

**PROVIDING BASIC GENETIC EDUCATION TO PARAMEDICAL/HEALTH
PROFESSIONALS AT SELECTED INDIAN OPHTHALMIC CENTERS**

by

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ABSTRACT

Introduction: In developed nations like the United States of America, genetic counselors help patients understand the health implications of genetic information. However, in developing countries, overwhelming patient volumes and a lack of genetic providers has hindered the progression of genetics as part of patient evaluation. The goal of the present study is to implement genetic education in locations where practicing genetic counselors are unavailable to aid the physician in patient management. This pilot study focuses on ophthalmic genetics in nine eye clinics throughout India that requested such an intervention as part of a national research group in 2011.

Methods: The project consisted of two phases: education and implementation. The educational phase involved the creation and dissemination of an online training course designed for paramedical and health professionals. The course focused on the basics of genetics, communication of genetic concepts, and how to construct a three-generation pedigree. Pre- and post-test assessments were used to assess efficacy. A field trip to India to conduct in-person course review workshops was completed. The implementation phase allowed participants to integrate skills from the course into clinical practice for 6 months. After the implementation period, a second, non-interventional field trip to India allowed for clinical observations of patient pathway, content of interaction, and clinical supervision. Site supervisors were asked for

feedback and to disclose any adverse events (defined as any negative event as a direct result of provision of genetic education) that occurred during the implementation period.

Results: Nine clinics in India completed the project. Average pre- and post-test score differences were statistically significant ($p < 0.05$) in all modules. While all 9 centers have used genetic education with consistency, with pedigree-taking being the most widely implemented practice, 7 of 9 have sustained its use. Clinical observations revealed that all participants can construct three-generation pedigrees and zero adverse events were reported.

Conclusion: This pilot project is significant to public health because demonstrates an effective method of teaching the study population basic aspects of clinical genetics and that safe implementation of these skills with perceived benefit is realistic. Sustained implementation depends on a distinct patient pathway with defined responsibilities.

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PREFACE

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1.0 INTRODUCTION

This is a pilot study that aims to introduce genetic education in eye centers where formally-trained genetic counselors and other genetic services are largely unavailable. We propose this to be possible by creating a subset of hospital employees (paramedical or other health professionals) as Genetic Educators through an online training course that teaches basic genetics as well as how to communicate the information to patients. Two major barriers to clinical genetics in developing countries are limited patient education and limited time. The purpose of Genetic Educators is informational in nature and they are not responsible for diagnosis, interpretation, or decision-making. This group of individuals is able to define and explain basic genetic terms to patients who may have minimal understanding, thereby preparing patients to receive inheritance counseling and medical evaluation from the physician. Genetic Educators are also trained to take detailed family histories in the form of a pedigree. This initial study takes place in eye clinics throughout India with the intent that the program can be modified to benefit other cultures and specialties in the future.

1.1 SPECIFIC AIMS

Plan: To design an online genetics education course for paramedical/health professionals in selected Indian ophthalmic centers with the intent to equip participants with the knowledge and

skills to provide patients with basic, clinically-relevant genetic information. The course is to be disseminated online to study participants. It is not a specific aim of this project to train individuals to act as genetic counselors.

Specific Aim 1: To create an online education program that is effective in teaching our study population the basics of human genetics and how to communicate genetic information with patients. In order to evaluate the online course's ability to increase participant knowledge of genetics, scores of pre- and post-test assessments are to be compared. The study staff hypothesizes a statistically significant difference between mean pre- and post-test scores for each module. This aim is to be furthered by the initial field trip to India to present the course review workshops in order to reinforce key concepts and to emphasize the role of the Genetic Educator.

Specific Aim 2: To have participants trained through the Genetic Educator Training Course implement the knowledge and skills into clinical practice. The study staff hypothesizes all centers will incorporate the training program uniquely in a way that benefits their current workflow. This is to be evaluated during the second, non-interventional field trip to India when Genetic Educator interactions are observed in clinic.

2.0 BACKGROUND AND SIGNIFICANCE

2.1 INTRODUCTION OF GENETIC COUNSELING

Clinical genetics is a rapidly-growing medical specialty in much of the developed world. The National Society of Genetic Counselors (NSGC) defines genetic counseling as the process of helping people understand and adapt to the medical, psychological, and familial implications of genetic contributions to disease. The process integrates i.) Interpretation of family and medical histories to assess the chance of disease occurrence or recurrence; ii.) Education about inheritance, testing, management, prevention, resources, and research; and iii.) Counseling to promote informed choices and adaptation to the risk or condition (Resta, *et al.*, 2006). Genetic counseling takes a holistic approach, but revolves around the core components of collection of family history, review of medical history, establishment or verification of diagnosis, risk assessment, education, decision support, informed consent, genetic testing, and psychological counseling (Hahn, 2011). The concept of being able to receive genetic information and diagnosis at the same time as routine medical care burdens the patient with fewer obligations, which increases medical continuity (Salo-Mullen and Guillem, 2012). Overall, giving patients understandable genetics information improves their quality of care (Marks, 2004).

A relatively new field, genetic counseling has grown from a primary focus in prenatal care to solid establishments in oncology, pediatric, and specialty practices (including

ophthalmology). In 2013, NSGC membership reached 2,960 individuals, reflecting the importance of giving genetics information to patients (Nagy, 2013).

2.2 GENETICS COUNSELING EDUCATION PROGRAMS

Since genetic counseling was established in the United States in the 1970s, at least 16 additional nations now offer Master's level education programs in genetic counseling. Nationally-recognized Master's degree programs exist in Canada, Cuba, the United Kingdom, the Netherlands, France, Spain, Portugal, Israel, Norway, Japan, Taiwan, Korea, the Philippines, Saudi Arabia, South Africa, and Australia (TAGC, 2011). Other countries, including Finland, China, and India, are working toward developing more formal training programs to benefit their healthcare systems (Edwards, 2010).

Genetic counseling education in much of North America and Europe must follow the guidelines and recommendations of established societies. These groups create proposed curriculums and core competencies for the profession. Both groups require the curriculum to include coursework on human genetics and psychosocial skills as well as clinical experiences through rotations under the supervision of genetic counselors (ACGC, 2014 and EBMG, 2014). North America currently has 35 graduate programs (USA: 32, Canada: 3) that offer Master's degrees in genetic counseling. These programs are either fully or provisionally accredited by the Accreditation Council for Genetic Counseling (ACGC) (ACGC, 2014). In Europe, the European Board of Medical Genetics (EBMG) Genetic Counsellor Division has granted approval for 5 genetic counseling Master's programs. Two of these programs are located in the United Kingdom, whereas France, Spain, and Portugal each have 1 program (EBMG, 2014).

Countries with available clinical genetics services may not necessarily offer formal, specialized training programs in medical genetics or genetic counseling. Some of the reasons for this include a heavy burden of population, limited resources, and lack of available personnel. Genetics professionals in many of these countries often train in outside countries and then return to work in their home country. For example, the nations of Iceland and Turkey do not have training programs in genetic counseling (Stefandottir, *et al.*, 2013; Yurdagül and Tekşen, 2013). Because of the small population size, Iceland does not have a graduate training program specifically for genetic counseling and depends on training programs in outside nations to train practicing counselors. In Iceland, genetic counseling technique is incorporated into the curriculums of medical and midwifery schools (Stefandottir, *et al.*, 2013).

2.3 GLOBAL CLINICAL GENETICS AND RESEARCH

2.3.1 Global Clinical Genetics Services

As clinical genetics in the United States of America and other nations continues to develop, expand, and specialize, its accessibility varies greatly worldwide. In the United States and Canada, genetics centers are often associated with academic settings where clinical services are integrated within the institutions (Battista, *et al.*, 2012).

This is replicated in other developed nations such as Iceland where genetic services have been offered since 2002, combining laboratory and clinical services in a central institute (Stefandottir, *et al.*, 2013). These services consist of 2 part-time medical geneticists, 1 full-time genetic counselor (formally trained at Cardiff University in the United Kingdom), 1 pediatric

medical geneticist and an oncologist also dedicates time to provide counseling for hereditary cancer syndromes. The population of Iceland is 325,671 and therefore a central institute is more easily accessible by everyone (Statistics Iceland, 2014).

While Cuba may not be considered a developed country economically, the medical infrastructure has allowed the implementation of genetics to reduce infant mortality caused by neural tube defects and to manage a founder population of sickle cell anemia, possibly related to the consanguinity rate which ranges from 1% to 11% nationwide (Cruz, 2013). By 1981, medical genetics grew beyond the capital city of Havana to a nationwide service (population: 11,047,251 (CIA, 2014)), to offer prenatal genetic services, targeted newborn screening, and targeted molecular diagnostics for conditions common in Cuba (Cruz, 2013).

Saudi Arabia is considered a developed country, with a population of 27,345,986 (CIA, 2014). It is highly conservative with traditions deeply rooted in Islam. One common social practice is consanguinity, which is estimated to be present in 56% of unions (Qadi, *et al.*, 2013). Therefore, Saudi Arabia developed genetic services and genetic counseling due to the increased risk for autosomal recessive disease. The incidences of hemoglobinopathies are particularly high and led to the establishment of mandatory premarital screening for sickle cell disease and β -thalassemia in 2005. Test results are connected electronically to marital courts and marriage certificates are only issued to couples that completed testing (Qadi, *et al.*, 2013).

In Turkey, healthcare, including the provision of genetic services, is controlled by the Ministry of Health (Yurdagül and Tekşen, 2013). In a population of 74.7 million, the consanguinity rate is greater than 20%. Genetic counseling is available through 41 Turkish institutions, although it is performed by physicians or medical geneticists and not by genetic counselors. The main genetics services offered in Turkey are preconception carrier screening,

prenatal genetics, newborn screening, and cancer screening. The carrier screening is mainly focused on sickle cell disease and β -thalassemia (Yurdagül and Tekşen, 2013).

2.3.2 Global Genetic Research Initiatives

Many countries conduct genetic research to establish areas of need in public health and medicine. Cuba is an example of such an approach, conducting epidemiological studies addressing disability screening and genetic causes of intellectual disability. The results of these studies were used to assess the demand for genetic counseling services (Cruz, 2013). Others maintain databases for future research or for ancestry purposes, and Iceland is an excellent example where databases are focused on large family histories, cancer diagnoses, and other research studies (Stefandottir, *et al.*, 2013).

2.3.3 Genetic Counseling In India

Genetic counseling is not a nationally recognized profession in India, as demonstrated by a lack of healthcare regulations or a professional organization. There are no organizations that establish requirements, guidelines, or core competencies in regards to who can provide genetic counseling and how it should be provided. Among the individuals that provide genetic counseling are clinical geneticists, ultrasound technicians, fetal medicine practitioners, pediatricians, gynecologists, and obstetricians (Elackett, 2013). These individuals may be trained abroad, trained informally, or self-trained. In this nation of 1.2 billion people, the 2nd largest in the world, there are 25 practicing genetic counselors (Elackett, 2013).

There has been an impetus to consider genetics as an aspect of public health in India with the motivation for disease prevention rather than treatment (Agarwal, 2009). In order to better establish clinical genetics, medical genetics information should be integrated into medical school curriculums as well as the creation of more specialized programs (Agarwal, 2009). Although there are no formal Master's degree programs in genetic counseling in India, there are two 1-year certificate programs. Of the 25 practicing genetic counselors in India, 4 trained at institutions abroad while the others obtained post-graduate certificates, offered within hospital systems in Hyderabad and Bangalore. The Hyderabad certificate program in genetic counseling at Kamineni Hospital was established in 2007 and is modeled after the University of California, Irvine program in the United States. The certificate program in Bangalore at Manipal Hospital was established more recently in 2012 and is modeled after the Griffith University program in Australia. For both Indian programs, there is less emphasis on psychosocial counseling as this is considered a skill less needed by genetic counselors in India (Elackett, 2013).

As far as other genetics professionals in India, there are 1,000 members of the Indian Society of Human Genetics, but only 50 of these individuals practice clinical genetics (Singh, et al., 2010). A total of 47 centers offer genetic diagnostic services including 40 that provide cytogenetic analysis, 28 that provide molecular testing, and 26 that provide prenatal diagnosis. Centers offering these services are responsible for varying numbers of patients ranging from 2.3 million to 83 million individuals per center (Singh, et al., 2010).

2.4 GLOBAL OPHTHALMOLOGY

2.4.1 Prevalence of Blindness

Blindness is a significant burden worldwide. In 2010, World Health Organization estimated that blindness, defined as best correctable vision of 20/400, affects approximately 39.4 million people globally. Another 246 million people are affected by low vision, defined as best correctable vision between 20/60 and 20/400 (Mariotti. 2010). Among children, the prevalence of blindness is approximately 0.7 in 1000 (Rahi, *et al.*, 1999). At least half of the cases of childhood blindness have a genetic cause (Graw, 2003). Although it is less common in children than in adults, childhood blindness has more long-term and widespread effects encompassing the family, education, employment, and social arenas (Rahi, *et al.*, 1999).

India contains a sizeable percentage of the world's blind. There are 320,000 blind children in India, which exceeds the number of blind children in any other country. This number is 22.86% of the world's blind children (Bhattacharjee, *et al.*, 2008). In total, India's blind inhabitants account for 20.5% of world blindness (with 8.1 million blind people), even though India's population only accounts for 17.5% of the world population. There a further 54.5 million people with low vision in India (Mariotti, 2010).

2.4.2 Financial Burden of Blindness

Blindness and low vision services also put a significant financial burden on society. A proposed method of quantifying the cost of the blind to society is the loss of gross national product (GNP) caused by inability to initiate or continue income-generating employment. Combining the effects

of childhood and adult blindness worldwide, this ranges from \$167.5 billion to \$243.9 billion USD yearly (Smith and Smith, 1996). This burden continues to grow as the world population and life expectancy both increase (WHO, 2006).

2.4.3 Congenital ocular malformations

Congenital ocular malformations occur with an incidence of 6 in 10,000 births (Siddiqui, *et al.*, 2012). While the cause of many ocular malformations remains unknown, genetic etiologies (single gene defects and chromosomal abnormalities) account for the majority of known causes, including 39.13% of all congenital ocular malformations (Bermejo and Martinez-Frías, 1998).

Studies in India have suggested rates of congenital ocular malformations ranging from 0.75 in 1,000 births to 10.5 in 1,000 births (Stoll, *et al.*, 1992; Singh, *et al.*, 1980). Reported incidence rates vary depend on study methodology and geographic region. In a study of 12,337 live births in South India, congenital ocular malformations occurred in 1.64 in 1,000 births, where microphthalmia was the most commonly seen anomaly (Ravikumara and Bhat, 1996). The incidences reported in India are generally comparable to incidences reported elsewhere. However, with a population of over 1.2 billion, the burden of ocular malformations is much more significant.

2.5 OPTHALMIC GENETICS

Approximately one-third of all genetic disorders include eye abnormalities and there are over 170 known heritable ocular genetic conditions (MacDonald, *et al.*, 2004; McKusick, *et al.*,

1994). However, because genetic eye disorders are specific in nature and therefore it is beneficial to have specialized genetic counselors with a deeper knowledge of ophthalmic conditions to best explain the details to patients in lay terms (Sutherland and Day, 2009). Even in developed countries such as Canada, this specialized genetic counseling service has an 18-month waiting list for individuals that need an appointment (Sutherland and Day, 2009).

The American Academy of Ophthalmology (AAO) has newly established guidelines for clinical genetic testing of inherited eye conditions. The AAO views genetic testing as a medical intervention with great potential benefit. However, it also involves some degree of risk and should be accompanied by skilled counseling (either by a knowledgeable physician or genetic counselor). A main recommendation is that if a physician lacks formal knowledge of genetics and genetic testing, a referral to a certified genetic counselor is advised (Stone, *et al.*, 2013).

3.0 METHODS

This was a descriptive and interventional pilot study approved by the University of Pittsburgh Institutional Review Board (IRB) with Exempt Status as an Educational Curriculum on March 26, 2013 (PRO13020479). A modification was approved on May 16, 2013 (See Appendix A). Letters of Permission were obtained from each center or hospital in India granting the University of Pittsburgh to conduct the present study. Each location met with an ethics review board individually and concluded that formal review for participation in the study was not required (See Appendix B). A diagram of the full study layout including participant actions is displayed in Figure 1.

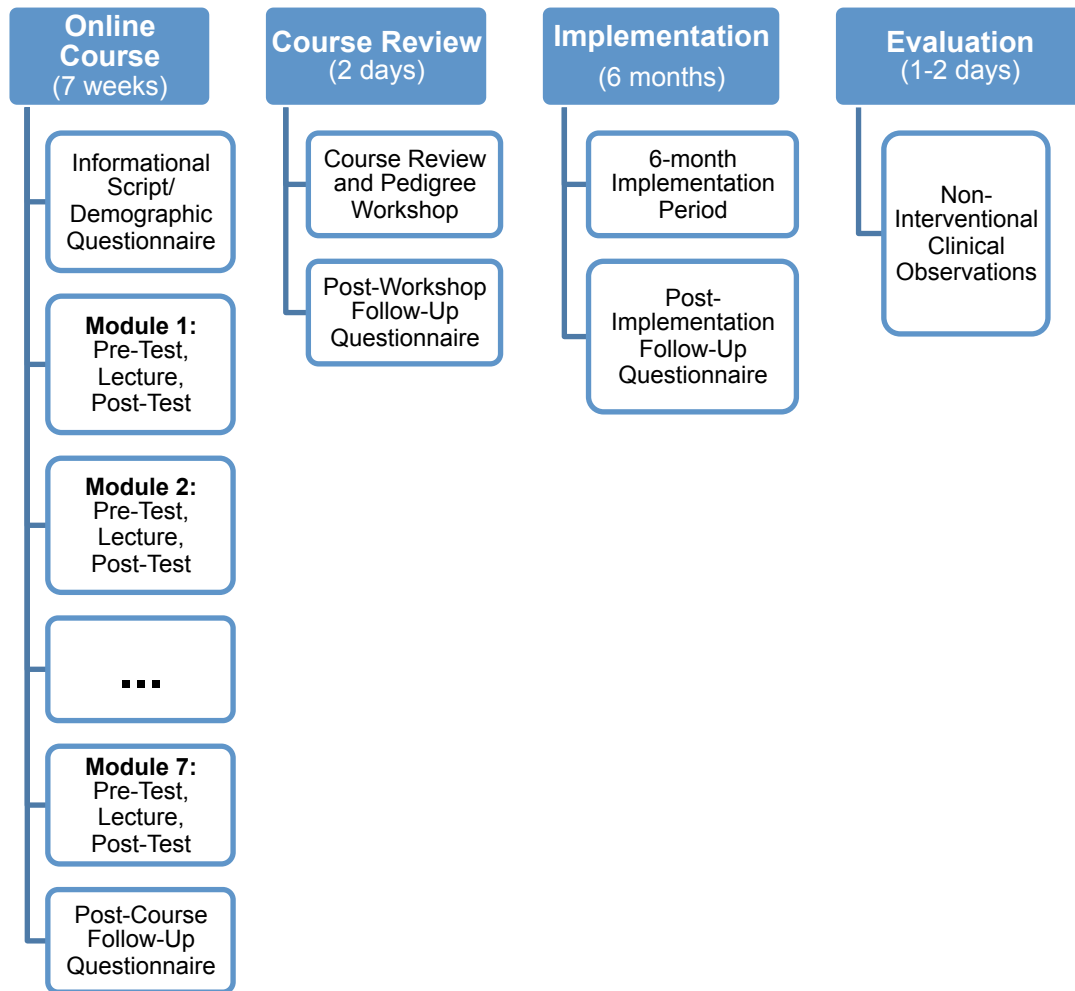


Figure 1. Layout of study schedule

3.1 SELECTION OF CENTERS AND PARTICIPANTS

Centers participating in this study had expressed interest in developing a component of genetic evaluation in their clinics and thus, participation was voluntary. Although ten centers expressed an interest, nine centers completed the project: Dr. Shroff Charity Eye Hospital in New Delhi, All India Institute of Medical Sciences (AIIMS) in New Delhi, LV Prasad Eye Institute (LVPEI) Main Campus in Hyderabad, LVPEI-Vizag Campus, LVPEI-Vijayawada Campus, LVPEI-Bhubaneswar Campus, Post Graduate Institute of Medical Education and Research (PGIMER) in Chandigarh, Aravind Eye Hospital in Madurai, and Narayana Nethralya in Bangalore.

Each center had one designated site supervisor who was asked to identify one to three individuals employed as paramedical or health professionals to participate. Since the course and other correspondence was to be in the English language, each participant was required to be able to read and understand English. In total, 26 individuals were given Study ID numbers to complete the online training course. During the course of the project, one participant and center withdrew from the study and one site supervisor left his position during the course of the study. Table 1 provides a summary of centers and participants for the online course and their locations in India (Figure 2).

Table 1. Centers participating in online course

| CITY | INSTITUTION | # OF PARTICIPANTS |
|----------------------------|---|--------------------------|
| Bangalore | Narayana Nethralya | 1 |
| Bhubaneswar | LVPEI-Bhubaneswar [†] | 3* |
| Chandigarh | PGI MER | 2* |
| Hyderabad | LVPEI-Main Campus [†] | 2 |
| Madurai | Aravind Eye Hospital | 4* |
| Mumbai | Aditya Jyot Foundation | 1 [‡] |
| New Delhi | All India Institute of Medical Sciences (AIIMS) | 3* |
| New Delhi | Dr Shroff Charity Eye Hospital | 4** |
| Vijayawada | LVPEI-Vijayawada [†] | 3* |
| Visakhapatnam | LVPEI-Vizag [†] | 3* |
| Total Participants: | | 26 |

* Indicates that a site supervisor (** = 2 supervisors) is included as a participant
The site supervisor at LVPEI-Bhubaneswar left his position during the present study
[†] LVPEI = LV Prasad Eye Institute
[‡] This participant was unable to attend review workshop and was excluded from data analysis after knowledge assessments



Figure 2. Map depicting locations of centers able to complete full study

3.1.1 Informed Consent

Since the current study was accepted under “Exempt Status,” formal informed consent was not required from participants. Participants were informed of the commitment expectations as well as risks and benefits of participation via a script that preceded the first page of the first online questionnaire (See Appendix C). As delineated by the University of Pittsburgh Institutional Review Board, the script included the following: the word “research,” expected study duration, subject responsibilities, risks and benefits, how confidentiality will be maintained, voluntariness and the ability to withdraw, and the e-mail address of a contact person.

3.2 ONLINE COURSE DEVELOPMENT

3.2.1 Module Topics and Information Presentation

A projected timeline for the online component of the study was seven weeks. The course, titled the Genetic Educator Training Course, was modular in format (seven modules in total) with each module available online for one week. The content of course modules 1 through 5 was based on major concepts in molecular, human, and ophthalmic genetics while modules 6 and 7 focused on interacting and communicating with patients. Titles of all modules are displayed in Table 2. The Core Competencies in Genetics for Health Professionals outlined by the National Coalition for Health Professional Education in Genetics (NCHPEG) were considered in the creation of the course and basic content from introductory undergraduate and graduate genetics courses was also included. Information was presented in clear and simple terms recognizing that English was not the first language of the participants.

Table 2. Module titles

| Module | Title |
|-----------------|---|
| Module 1 | Molecular Biology |
| Module 2 | Cell Cycle & Genetics |
| Module 3 | Inheritance |
| Module 4 | Mutations and Genetic Testing |
| Module 5 | Inherited Congenital Anomalies of the Eye |
| Module 6 | Talking to a Patient I: Patient Education Basics |
| Module 7 | Talking to a Patient II: Taking a Family Pedigree |

An international advisory committee was formed in order to ensure that all material within the course lectures was accurate, easily understandable, and culturally sensitive. The advisory committee consisted of 6 individuals: 2 pediatric ophthalmologists (one practicing in the USA, one practicing in Portugal), 2 ophthalmic genetic counselors, a medical geneticist that previously practiced ophthalmology in India, and a genetic counseling program director that has conducted extensive research in India. These individuals were integral in creating an informative course that was culturally sensitive. Examples of edits included removal of American slang language and presenting X-linked inheritance in a more objective fashion that minimized the possibility of guilt and blame of females. In addition to the advisory committee, we were also in contact with site supervisors that helped devise the timeline and logistics of the project. This helped ensure that the course was realistic for participants.

The modules were narrated, animated lectures created using Microsoft PowerPoint and converted into video files (See Appendix D). This presentation allowed participants to both hear and see the written language to maximize understanding and accommodate different individual learning styles. Each module began with a title slide followed by a slide outlining the purpose and objectives for the current module. The remaining slides included informational text accompanied by simple illustrations and animations when possible. The lectures were posted as videos and participants were able to pause and rewind in order to repeat portions as needed. Video lengths ranged from roughly 7 minutes to roughly 19 minutes.

3.2.2 Generation of Study ID Numbers

Study ID numbers were used to as a way to track responses over the course of the project. ID numbers were created and assigned to each participant using an online random number generator

(http://www.mathgoodies.com/calculators/random_no_custom.html). Each number was generated using a lower limit of 1000 and an upper limit of 1999. Participants were informed of their study ID numbers via email along with the initial information regarding participation in the online course. Participants were required to enter their assigned number at the beginning of each online questionnaire.

3.2.3 Questionnaires

Questionnaires included a demographic questionnaire, pre- and post-test knowledge assessments for each module (1-7), and follow-up questionnaires. (See Appendix E for knowledge assessments and Appendix F for demographic and follow-up questionnaires). All questionnaires were created for the purposes of this study. None of the surveys were validated largely due to the inclusion of fact-based questions. The questionnaires were posted online via SurveyMonkey®, a website easily accessible to participants. The first question in each survey asked for participant Study ID numbers so that responses could be correlated to the correct individual and reminders could be sent for completion of tasks.

The demographic questionnaire was distributed to participants at the beginning of the 7-week course, immediately before Module 1. This questionnaire gathered information about participants' history (education, job title, number of years employed), practice (patient volume per day), and knowledge and comfort levels regarding genetics.

Each online module was preceded by a 15-question pre-test knowledge assessment and followed by the same 15-question post-test assessment. This allowed a comparison between baseline knowledge and knowledge gained following the educational presentations.

Identical follow-up questionnaires were repeated at three time points: immediately following the 7th and final online module (“post-course”), following the course review workshops (“post-workshop”), and after the study staff observed utilization of skills in the clinic (“final”). The follow-up questionnaire echoed many questions from the demographic questionnaire, in order to determine if answers regarding patient volume, comfort, and knowledge of genetics changed, and if so, at which time point. These questionnaires also included an additional section of questions that serve as a course evaluation. Using a Likert scale, a previously validated method of measuring attitudes (Likert, 1932), participants were asked to describe how the training program affected their professional development, understanding of genetics, communication skills, and confidence, as well as their opinions on genetics and integrating the practice into their workflow. The response categories were as follows: 1 = Strongly Disagree; 2 = Moderately Disagree; 3 = Neutral/Don’t Know; 4 = Moderately Agree; 5 = Strongly Agree.

3.2.4 Webpage Hosts and User Interface

Materials were hosted online through two websites due to differences in Information Technology permissions between participating centers. Both websites created URLs (2 per week) only accessible by having the link and not able to be navigated to through the main website homepages. These hosts were World Society of Paediatric Ophthalmology and Strabismus (WSPOS) as an Area of Research Collaboration (aRc) and University of Pittsburgh Graduate School of Public Health’s Department of Human Genetics. All questionnaires including pre- and post-test knowledge assessments, demographic questionnaires, and follow-up questionnaires were created and housed online through SurveyMonkey® (<http://www.surveymonkey.com>).

Participants were emailed weekly with URLs to a landing page for the current module, with the option to complete the module through either WSPOS or the Department of Human Genetics. The landing pages provided a link to the SurveyMonkey® pre-test knowledge assessment. At the conclusion of the pre-test survey, users were automatically redirected to the website containing the educational video presentation and links to the SurveyMonkey® post-test knowledge assessment. Finally, users were re-directed back to the original landing page to confirm that they had completed all actions necessary for the module.

Module completion was tracked using Study ID numbers in SurveyMonkey® results. Individuals who had not completed the current module were sent up to two reminder emails per week, as necessary. Once all post-test assessments were completed, participants were emailed with their score expressed both as number correct out of 15 and as a percent. Answer keys were attached to result emails that included justification for each correct answer and explanation for each incorrect answer (See Appendix E).

3.3 ACTIVITIES IN INDIA

3.3.1 Course Review Workshops

Following the 7-week online course, the study staff traveled to India to offer two-day course review workshops in two locations. Participants and supervisors were asked to attend the location that was most convenient for them. One workshop was held in southern India in Hyderabad at LV Prasad Eye Institute's Main Campus and one in northern India in New Delhi at Dr Shroff Charity Eye Hospital. It was important that the information be reviewed, but more

important for participants to understand the duties and limitations associated with the Genetic Educator role.

Prior to the workshops, participants were asked to complete a short survey to identify the three course modules that were the most challenging. Data was collected separately for each location. This information was used to indicate which modules should be addressed more intensely during the review. However, all modules were reviewed at both workshops with particular emphasis on collecting pedigrees. Centers were also requested to formally delineate current patient pathways and their proposed pathways to incorporate genetic education.

A major portion of the format was reviewing the training course slides, interjecting multiple-choice questions to assess retention of important concepts. Participants were also broken into partners and small groups to do some communication activities. They were asked to discuss how they might explain genetic concepts to patients (chromosomes, gene, inheritance patterns, etc.) and to then present it to the full group. The last piece of the review workshop was to practice eliciting pedigrees from a patient. Pre-conceptualized scenarios were role-played between participants in pairs and as a group with study staff and participants. This focused on using accurate pedigree notation and symbols and asking the right questions appropriately to collect the necessary information.

Following the workshop, participants were asked to complete the follow-up questionnaire second time. Additionally, participants that successfully completed all 7 online educational modules and attended a review workshop received a certificate of completion (See Appendix G). Certificates were emailed to site supervisors to distribute amongst the participants at their centers.

3.3.2 Clinical Observations

After the review workshops, sites were asked to implement genetic education into their workflow to the extent they were comfortable. It was suggested for the purposes of personal audit that each participating center keep a de-identified logbook of patients that received genetic education. Approximately six months after implementation, the study staff traveled to India to observe Genetic Educators interacting with patients at 6 sites: PGIMER in Chandigarh, Dr Shroff Charity Eye Hospital and AIIMS in New Delhi, Aravind Eye Hospital in Madurai, LVPEI-Main Campus in Hyderabad, and Narayana Nethralya in Bangalore. Two sites (LVPEI-Bhubaneswar and LVPEI-Vijayawada) that could not be physically visited due to time and financial constraints had evaluations via teleconference. Genetic educators from LVPEI-Vizag traveled to LVPEI-Main Campus for assessment.

The purpose of clinical observations was to assess the patient pathway including routine of referral, presence or absence of dedicated space, relationship of site supervisor to educator, method of pedigree obtainment, and content of the interaction. Site supervisors were also asked to disclose any occurrences of adverse events, defined as any negative event occurring as a direct result of genetic education during the 6-month implementation period. Clinical visits also allowed for the opportunity for participants and supervisors to comment on their experiences and perceived impact of the project.

3.4 STATISTICAL ANALYSIS

Statistical analysis was performed on responses to SurveyMonkey® questionnaires using descriptive statistics. SurveyMonkey® tabulates some basic statistics automatically such as averaging response values and the remaining tests were performed using Microsoft Excel®.

First, knowledge assessment scores were examined to determine if there was a significant difference between pre- and post-test knowledge assessment scores. For each educational module, the mean pre-test score was compared with the mean post-test score using two-tailed t-tests, where significance was defined as a p-value of less than 0.05.

Likert scale questions in the series of follow-up questionnaires were assessed by frequency and averaged. Two-tailed t-tests were performed to compare responses to the same questions between different time points. Although the questionnaires asked participants to rank their agreement with statements using a scale from 1 (Strongly Disagree) to 5 (Strongly Agree), the rating scale used for statistical analysis was as following: 0=Strongly Disagree, 1=Moderately Disagree, 2=Neutral/Don't know, 3=Moderately Agree, 4=Strongly Agree. This statistical rating scale was used to be consistent with the statistical analysis of other questions in this study. Again, significance was defined as a p-value of less than 0.05.

4.0 RESULTS

4.1 DEMOGRAPHICS

4.1.1 Education

The demographic survey revealed the highest level of formal education achieved by study participants and is summarized in Table 3. The most common education level achieved by participants was a Bachelor's degree in Optometry or Ophthalmic Techniques (11 out of 26, 42.3%).

Table 3. Participant demographics: Education

| HIGHEST LEVEL OF EDUCATION | # OF PARTICIPANTS |
|--|-------------------|
| Higher secondary | 1 |
| Diploma in Optometry | 3 |
| Bachelor's Degree | 11 |
| Optometry or Ophthalmic Techniques (9) | |
| Nursing (1) | |
| Physics (1) | |
| Master's Degree | 3 |
| Optometry or Ophthalmology (2) | |
| Sociology (1) | |
| PhD | 2 |
| MD in Ophthalmology | 4 |
| Fellowship in Pediatric Ophthalmology | 1 |
| DNB, FRCS | 1 |
| Total Participants | 26 |

4.1.2 Workplace

Participants were asked about their current employment status. Job titles among participants included consultant, optometrist, ophthalmologist, professor, intern, scientist, sister (equivalent to nurse), and technician. The number of years employed at current workplace averaged 6.19 years, ranging from 0 to 18 years.

Participants were asked to estimate the number of total patients seen per day at their clinic or institute. The average patient volume was 196 patients per day; however, there was a wide range in responses, with estimates from 5 to 1,000 patients per day. When asked how many patients per day a participant was individually responsible for, the average patient load was 34 patients per day.

4.1.3 Baseline Genetics Knowledge and Practice

The demographic questionnaire, administered prior to the modular course was a baseline assessment of the participants' current knowledge and practice of genetics.

First, participants were asked to rank their knowledge of genetics, ranging from No Knowledge, Very Poor, Satisfactory, Good, to Very Good (Figure 3). The most frequent answer was “Satisfactory,” accounting for 42.3% (11 of 26) of responses. The remaining answers represented a lower self-assessment of knowledge (11 of 26, 42.3%) than a high self-assessment of knowledge (4 of 26, 15.4%). Of note, no participants considered their current knowledge of genetics to be “Very Good.”



Figure 3. Demographic questionnaire: Response to “How would you rank your knowledge of genetics?”

Participants were asked if they received formal genetics education. Of the 26 participants, 3 (11.5%) reported formal training, in which a one-year ocular genetics fellowship and a genetics Master’s program were specified. Twenty-three participants (88.5%) reported no formal training.

To assess the availability of genetic services in the selected institutions prior to this project, participants were asked if they were aware of any genetics clinics within their workplace. Twelve out of 26 (46.2%) were aware of a genetics clinic in their institute and 14 out of 26 (53.8%) were not aware of such a clinic.

Participants were asked to rate their comfort approaching genetic issues with patients, ranging from Very Comfortable, Comfortable, Neither Comfortable Nor Uncomfortable, Uncomfortable, or Very Uncomfortable (Figure 4). Fourteen of 26 participants (53.8%) indicated they felt “Comfortable” approaching these issues. Of note, one participant (3.8%) reported to be “Very Comfortable” discussing genetics issues with patients. Nine participants (34.6%) reported being “Neither Comfortable Nor Uncomfortable,” 2 participants (7.7%) reported being “Uncomfortable,” while zero participants reported being “Very uncomfortable.”

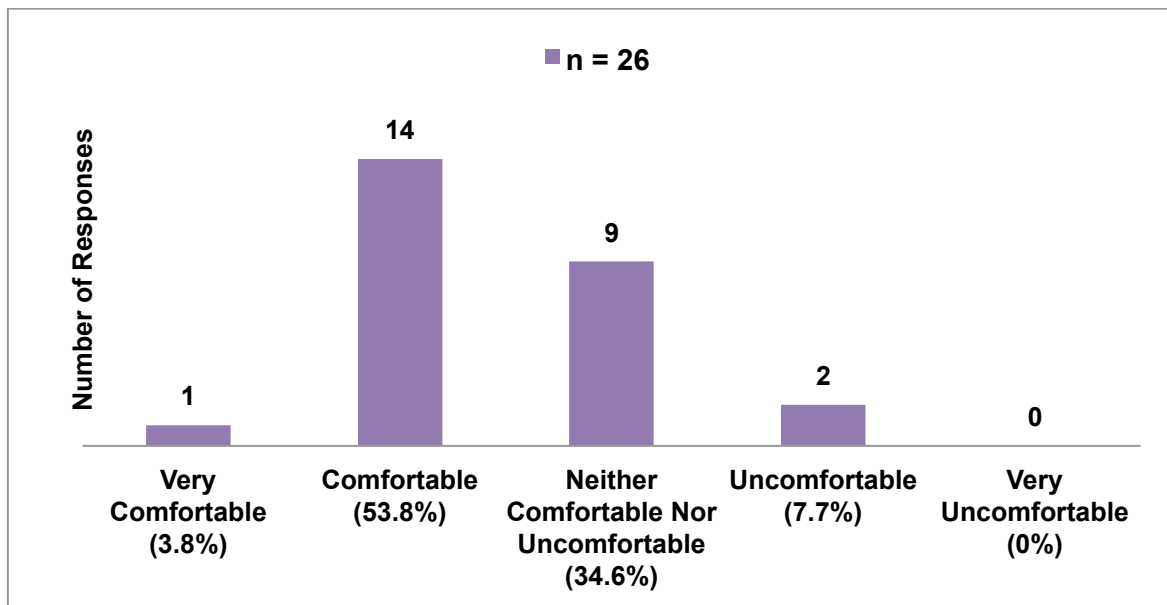


Figure 4. Demographic questionnaire: Response to “In general, how comfortable do you feel with dealing with genetics issues with your patients?”

Last, two items asked participants about their current clinical practice, including the frequency of collecting family health histories and discussing genetics with patients. Regarding the frequency of collecting health histories, the most common answer was “Always,” chosen by 11 out of 26 individuals (42.3%). Nine participants (34.6%) reported collecting family histories “Often,” 5 participants (19.2%) reported “Sometimes,” and 1 participant (3.8%) specified “Never.” All responses are shown in Figure 5. Regarding the frequency of discussing genetics with patients, the most commonly selected answers were “Only if the patient has a genetic condition” (8 of 26, 30.8%), and “Occasionally, but only if there seems to be a good reason for it” (7 of 26, 26.9%). One participant (3.8%) reported “Never,” 5 participants (19.2%) reported “Often, whenever it seems appropriate,” 3 participants (11.5%) reported “Mostly it is my usual practice,” and 2 participants (7.7%) reported “Almost always, with almost all patients when taking a medical history.” All responses to this question are shown in Figure 6.

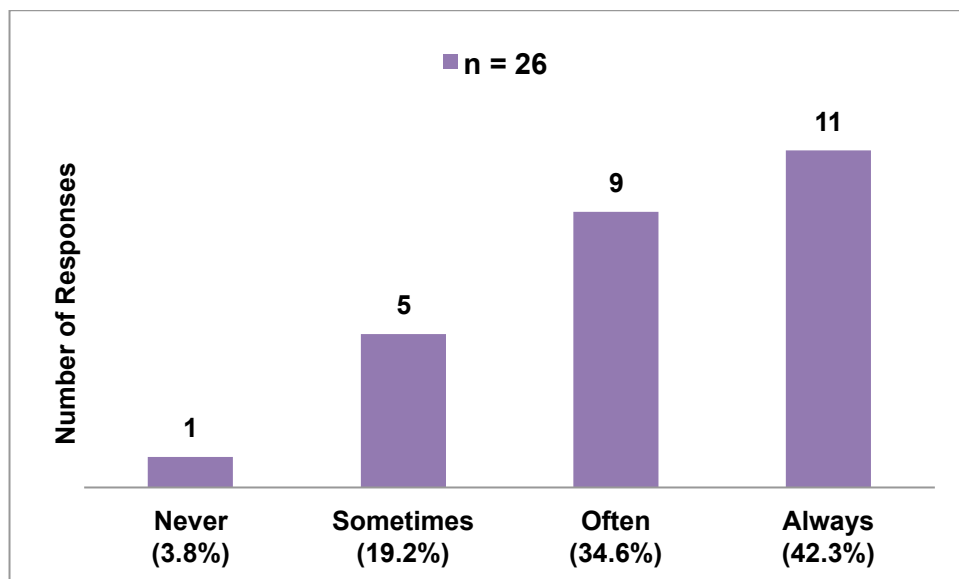


Figure 5. Demographic questionnaire: Response to “How often do you complete a family history for a new patient?”

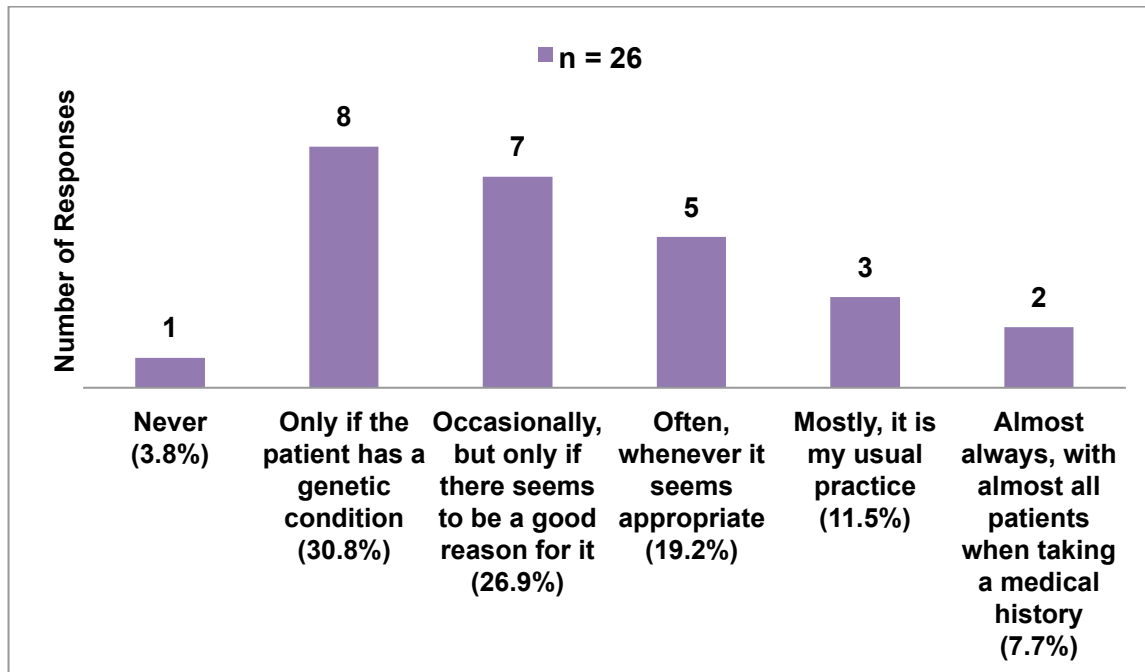


Figure 6. Demographic questionnaire: Response to “In your practice, how often do you discuss genetics with a patient?”

4.2 MODULE KNOWLEDGE ASSESSMENTS

Throughout the educational course, 7 knowledge assessments were administered before and after each module. All assessments included 15 fact-based items, which were identical pre- and post-module. All 26 course participants successfully completed all of the pre-test and post-test knowledge assessments.

For each module, the pre-test and post-test scores were calculated for each participant and average pre-test and average post-test scores were calculated among all participants. Each correct response was given a value of 1. The number of correct responses for each participant was summed, resulting in a potential maximum score of 15 for each assessment. In order to

determine whether scores differed between pre-test and post-test assessments, a two-tailed t-test was performed. Statistical significance was indicated by a p-value less than 0.05. The test scores for each module are shown in Figure 7. All seven modules showed a statistically significant difference between average pre-test scores and average post-test scores, where the post-test demonstrated higher scores.

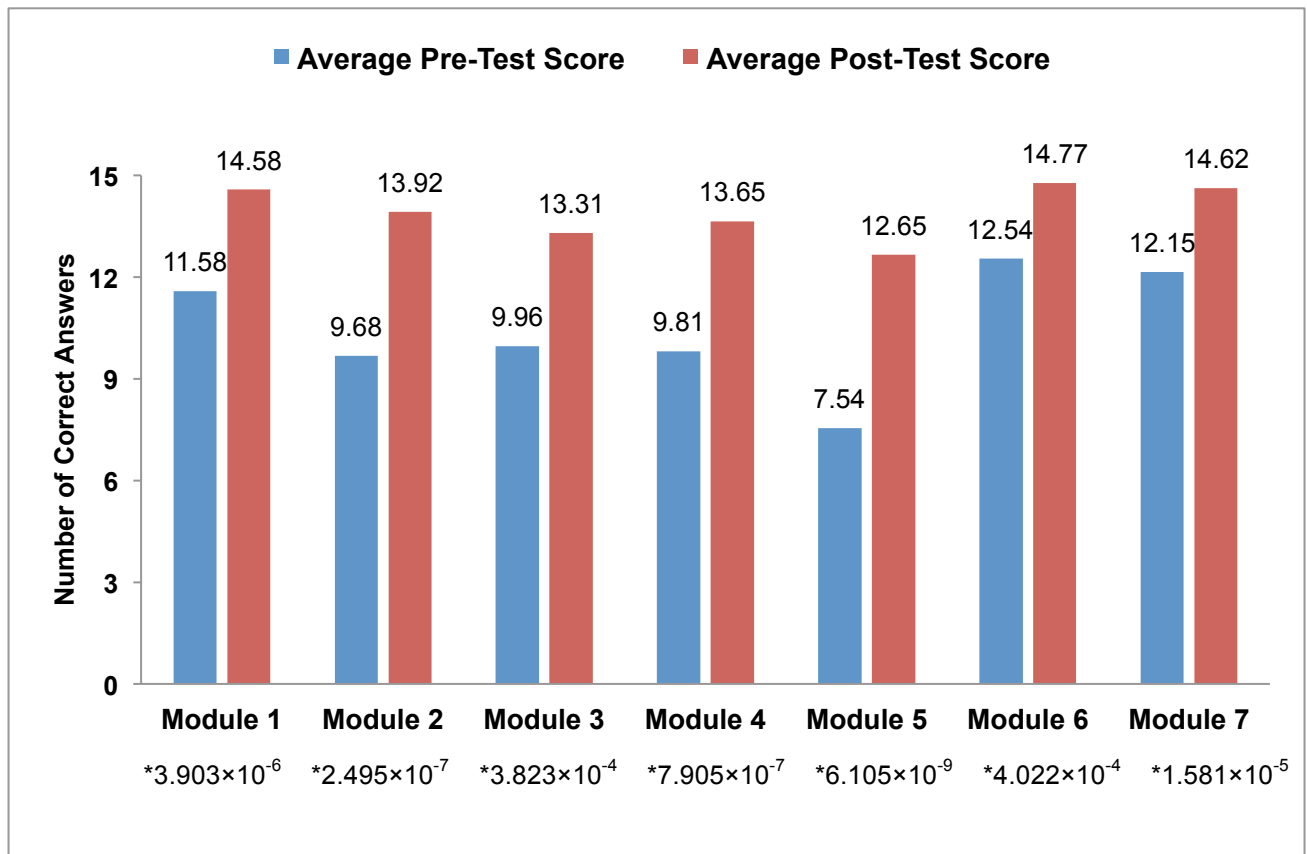


Figure 7. Summary of knowledge assessment scores.
P-values for each module are indicated below module number. * indicates statistical significance.

4.3 REVIEW WORKSHOPS

The first field trip to India (to Hyderabad and New Delhi) occurred 1 week after participants completed the online course. At the Hyderabad workshop, 15 individuals (participants and site supervisors) attended the workshop in person and 3 individuals attended via teleconference. At the New Delhi workshop, 7 individuals were present.

The workshops focused on reviewing the course, including slideshow presentations of the information presented in each module. Multiple-choice questions were distributed throughout each module for reinforcement. The questions did not repeat those that were asked on the knowledge assessment questionnaires. As part of the course debriefing, role-playing of drawing complex pedigree was performed but no data was actively collected.

4.4 CLINICAL OBSERVATIONS

4.4.1 Overview

Clinical observations were carried out by the study staff 6 months after genetic education was initiated in the clinics. Genetic Educators from all 9 sites were observed totaling 16 in number (the 9 site supervisors were not observed and 1 original participant from the online course failed to complete all requirements). The Genetic Educators were observed in person at 6 sites (Dr Shroff Charity Eye Hospital, AIIMS, Aravind Eye Hospital, Narayana Nethralya, PGIMER, and LVPEI-Main Campus). The Genetic Educators from the LVPEI-Vizag satellite location traveled to LVPEI-Main Campus in Hyderabad to see patients and be observed. The Genetic Educators

from the remaining 2 LVPEI satellite locations (Vijayawada and Bhubaneswar) were observed through video teleconference. The staff observed 16 Genetic Educators interact with 2-4 patients, depending on the clinic load. In total, 45 patient encounters were observed over the course of the trip.

It was noted how each center was implementing genetic education into their workflow and comments from participants and supervisors were collected regarding their experience with the project as well as its perceived impact. Supervisors also expressed their thoughts on potential future studies or extension studies regarding genetic education.

Although not a requirement, some centers tracked patient interactions with Genetic Educators during the implementation period through de-identified logbooks. Across all centers, the logbooks documented a total of 497 patient encounters.

4.4.2 Workflow

Each site utilized Genetic Educators in a manner that was appropriate based on clinic responsibilities and workflow, as determined by site supervisors. Descriptions of patient pathways for each participating center are summarized in Table 4.

Table 4. Patient pathways at participating centers

| |
|--|
| <p>AIIMS*</p> <p>Genetic Educator seeks patients in separate clinic → Pedigree taken in private, but not dedicated room → Pedigrees kept in notebook, not in patient chart</p> |
| <p>Aravind Eye Hospital (Genetics Clinic held 2 days/week)</p> <p>Referral (physician may draw out pedigree relationships) → Pedigree taken (or health history elicited for each individual on pedigree drawn by physician) in private, dedicated room</p> |
| <p>Dr Shroff Charity Eye Hospital (Genetic Educators each see patients 2 days/week)</p> <p>Referral → Genetic Educator appointment created → Pedigree taken and explanation of genetic concepts as necessary in private, dedicated room → Pedigree placed in patient chart → Patient attends remaining appointments</p> |
| <p>LVPEI (4 locations)*</p> <p>Referral → Pedigree taken (often while dilating or during imaging appointments) in private, but not dedicated room → Pedigree placed in patient chart → Physician documents pedigree is done and provides interpretation</p> |
| <p>Narayana Nethralya*</p> <p>Genetic Educator travels from remote location as needed → Pedigree taken in a private, but not dedicated room → Pedigree not maintained in patient chart → Blood drawn for future genetic studies</p> |
| <p>PGIMER (Genetic Educator sees patients for a half day on Fridays)</p> <p>Referral → Genetic Educator reviews chart → Pedigree taken in semi-private, dedicated room → Pedigree placed in patient chart → Patient returns to waiting room for other appointments → Physician reviews pedigree and provides necessary counseling</p> |

* These locations do not have a specific time dedicated to genetic education.

4.4.3 Pedigrees

For the centers that have been using genetic education, pedigrees are the most commonly applied skill in clinic. A majority of the sites (7 out of 9) maintained pedigrees created by Genetic Educators as part of the patient's permanent medical record. Dr Shroff Charity Eye Hospital created its own standardized pedigree form, which is used for all genetic education patients (See Appendix H).

All Genetic Educators were observed taking pedigrees. Of the 45 patient encounters observed, 45 3-generation pedigrees were obtained (100%). In encounters, ocular histories on family members were elicited (100%) and 32 encounters (71.1%) included additional, extra-ocular information. Eleven of 45 encounters (24.4%) elicited information about miscarriages and 39 of 45 encounters (86.7%) elicited information about consanguinity.

4.4.4 Impact

Through conversation and informal interview with Genetic Educators and site supervisors, the perceived impacts of the project were collected on observation visit days. These informal interviews were performed based on availability and thus not all participating individuals were available to answer each question. Genetic Educators or site supervisors from 7 out of 9 centers expressed that implementing genetic education has benefited their clinic or patient population in some capacity. PGIMER stated that it increased awareness of genetics among physicians and fellows, as they are now identifying patients for whom genetic education is appropriate. Four site supervisors stated that it has increased the overall efficiency and throughput of the clinic. No site supervisor volunteered the need to repeat pedigrees taken by Genetic Educators.

Implementation of genetic education has also been perceived to benefit the patients. Prior to implementation, patients had little to no awareness of genetics. It was also mentioned that it enabled clinicians to reach out to other family members that may need ophthalmic evaluation; a striking example of this was at PGIMER, where systematic pedigree taking allowed clinics to identify a large pedigree with developmental glaucoma and affected individuals were being seen by up to 5 different attendings. Once this scenario was realized, the family members were able to see the same ophthalmologist who was able to personalize treatment as a result.

Negative impacts were also reported. The site supervisor at AIIMS feels that Genetic Educators are currently interrupting the clinic because an established workflow has not been put into place, speculating that an established workflow would allow them to see a greater positive impact. The Genetic Educator trainees at AIIMS feel that their current workload is too great for implementation at this time but would be possible once a pathway is established and more trainees are added.

There is also a notion that this research project has large potential impact for the future. The site supervisor from AIIMS felt that the results of this study may be used as “ammunition” to justify further development of clinical genetics in Indian ophthalmic centers.

4.4.5 Genetic Educator Feedback

Genetic Educators were asked to provide open-ended feedback about all aspects of the project. The Genetic Educators feel that they are increasing their professional skill sets and feel value in doing so. They feel they are becoming better at obtaining relevant histories compared to before the project when they were only asking basic questions about the proband. As they continue to practice, they are becoming more comfortable in their role and are able to ask more sophisticated

questions to collect better information. At least 3 Genetic Educators expressed interest furthering their education by pursuing formal training in either medical genetics or genetic counseling.

The Genetic Educators noted challenges that they have experienced over the course of the project. Genetic Educators expressed difficulty in addressing miscarriages and consanguinity while taking a pedigree. They expressed interest in learning different approaches in how to broach these topics because while they may be uncomfortable, they are crucial for accurate pedigree interpretation. They also felt that introducing the purpose of the pedigree to the patient is a challenge. Sometimes it was difficult for the patient to understand the utility of this form of history taking. Lastly, they have had issues when patients with home internet access attempt to seek out information on diagnoses. This often led to patients asking complex questions which must be deflected to the physician.

4.4.6 Site Supervisor Feedback

In addition to elaborating on the perceived impact of the course, site supervisors were asked about their level of confidence in interpretation of pedigrees. They were also asked for general, open-ended feedback. These informal interviews were performed based on the availability of the supervisors and thus not all supervisors were available to answer each question.

Most supervisors were interested in a course designed specifically for ophthalmologists on pedigree interpretation (5 centers). The primary goal of this course would be to maximize the clinical utility of the pedigrees obtained by Genetic Educators. Two supervisors, with formal training in genetics, did not feel this would be of personal benefit, but one indicated that it would be of benefit to other physicians at his institute.

Interest was also expressed for repeating this course so that the centers can increase their number of trained Genetic Educators. Three centers were interested in growing their number of trained Genetic Educators. The supervisor of LVPEI-Main Campus stated that he envisions running his clinic with 7-8 Genetic Educators. Four centers (AIIMS, Dr Shroff Charity Eye Hospital, LVPEI-Main Campus, and LVPEI-Vizag) suggested that when repeating the course, more emphasis should be placed on pedigrees and less emphasis on the molecular basis of genetics. The supervisor from AIIMS thought it would be beneficial to have the course presented in person, rather than online. The suggestion entailed offering a two-day in-person course at 3 times so that multiple individuals from a center could participate without having to cancel full clinic days.

4.5 FOLLOW-UP QUESTIONNAIRE SERIES

4.5.1 Response Rate

The series of three follow-up questionnaires were distributed post-course, post-workshop, and post-observations (final). All 26 participants (100%) completed the post-course questionnaire, 23 participants completed the post-workshop questionnaire (88.5%), and 25 participants (96.2%) completed the final questionnaire.

4.5.2 Patient Volume

The three follow-up questionnaires in conjunction with the demographic questionnaire were designed to evaluate the effect of added genetic education tasks on average patient volume. The average number of patients seen by each individual per day (34 patients) remained the same after 6 months of implementation as it was prior to the initiation of this project.

4.5.3 Genetics Knowledge, Comfort, and Practice

The series of 3 follow-up questionnaires repeated the questions from the demographic questionnaire regarding genetics knowledge, comfort, and practice. The repeated questions were “How would you rank your knowledge of genetics?”, “How comfortable do you feel with dealing with genetics issues with your patients?”, “How often do you complete a family history for a new patient?”, and “In your practice, how often do you discuss genetics with a patient?”. Responses to each question were compared using two-tailed t-tests (with statistical significance defined as a p-value less than 0.05) to see if responses were significantly different at separate time points. T-tests compared the following time points: (1) demographic and post-course, (2) post-course and post-workshop, and (3) post-workshop and final. For statistical analysis, the most negative response category was scored as 0 and increased in increments of 1 for each subsequent response category.

Two t-tests yielded statistical significance. First, responses to the question “How would you rank your knowledge of genetics” in the demographic questionnaire were significantly different than the responses to the question in the post-course questionnaire. Comparison of responses between these time points showed that the average knowledge of genetics among

participants was significantly higher at the time of the post-course questionnaire as compared to the demographic questionnaire ($p=7.31 \times 10^{-7}$). Second, the responses to the question “How comfortable do you feel with dealing with genetics issues with your patients?” in the demographic questionnaire were significantly different than the responses to the question in the post-course questionnaire. Comparison of responses between these time points showed that the average knowledge of genetics among participants was significantly higher at the time of the post-course questionnaire as compared to the demographic questionnaire ($p=1.19 \times 10^{-4}$).

These significant values are indicated in the following table using an asterisk (*). All other t-tests did not show statistical significance at any time point. A breakdown of these questions examining the proportion of positive responses is available in Figures 8-11 and complete summary of responses is available in Table 5.

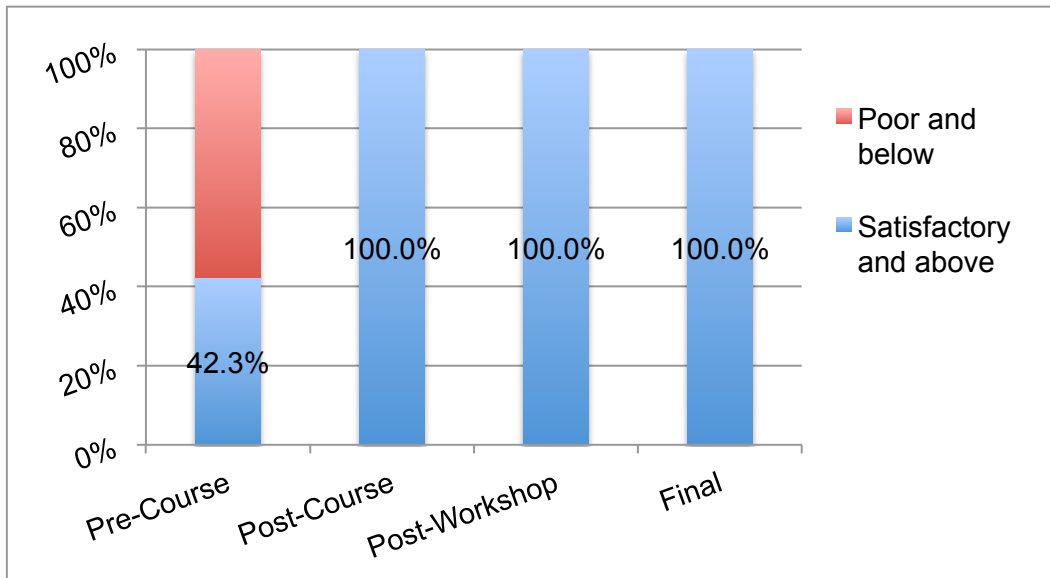


Figure 8. Analysis of responses to How would you rank your knowledge of genetics?

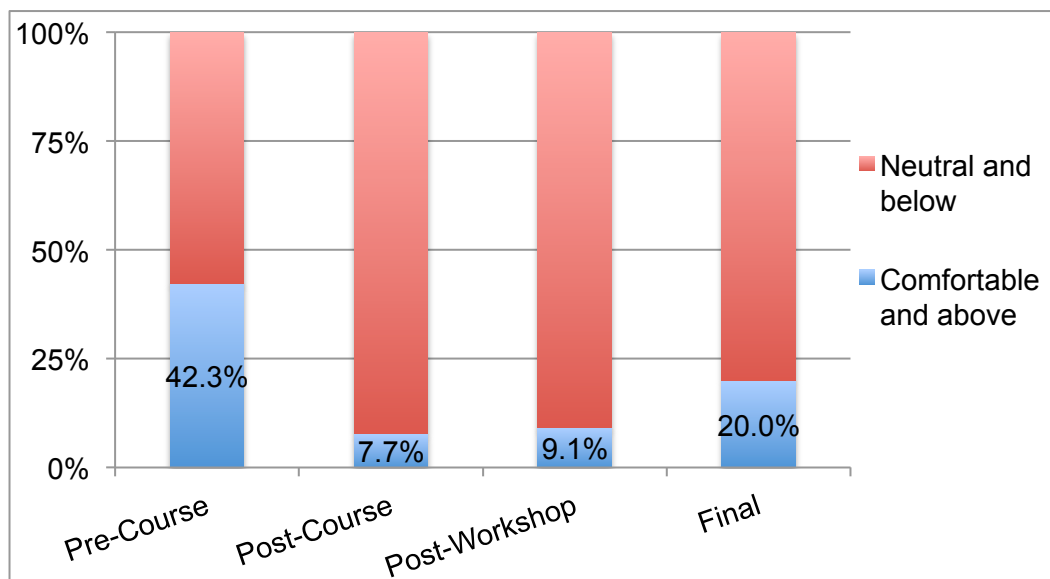


Figure 9. Analysis of responses to How comfortable do you feel with dealing with genetics issues with your patients?

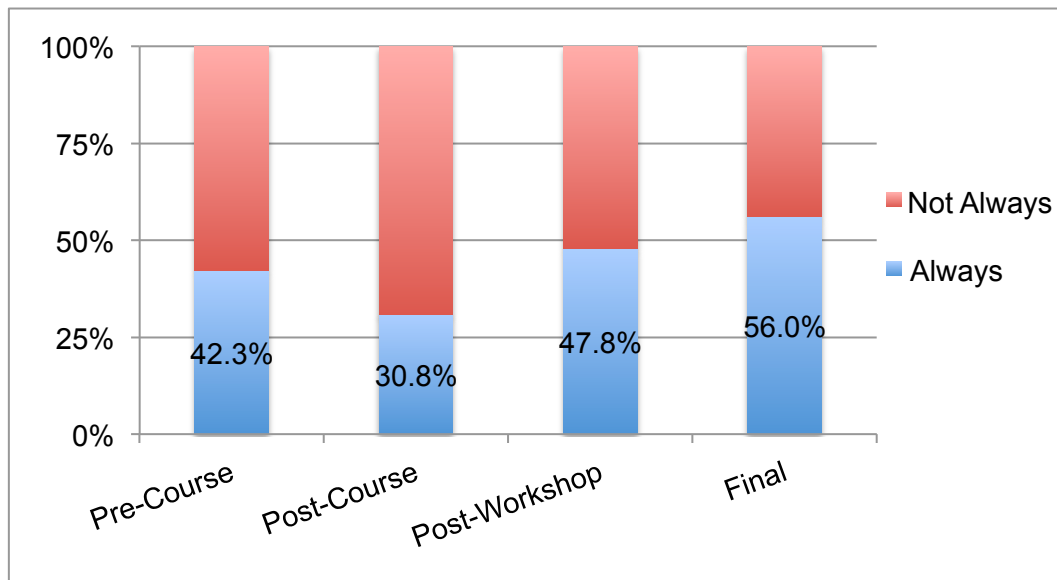


Figure 10. Analysis of responses to How often do you complete a family history for a new patient?

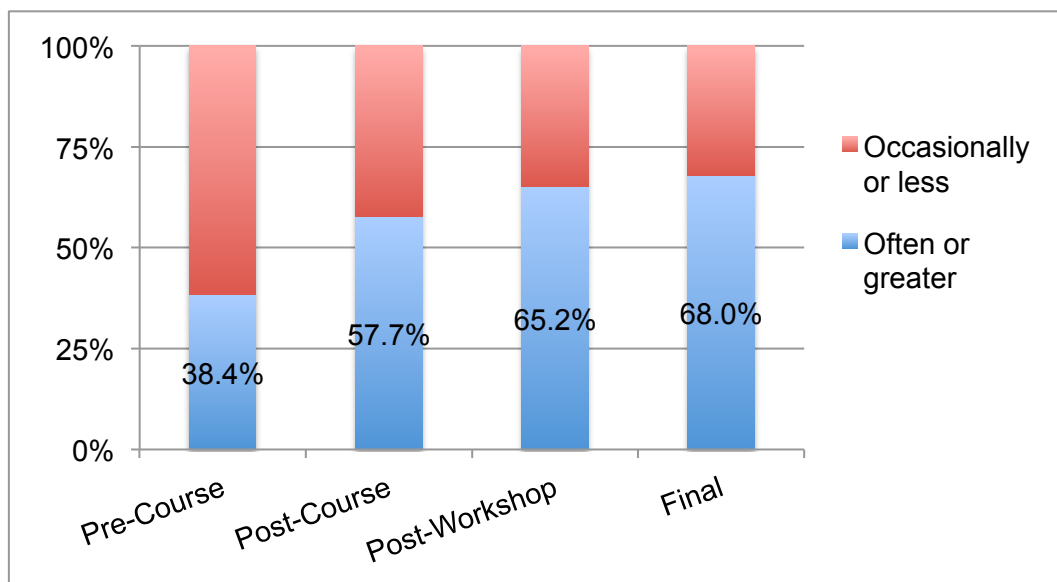


Figure 11. Analysis of responses to In your practice, how often do you discuss genetics with a patient?

Table 5. Responses to selected questions from demographic and follow-up questionnaires

| How would you rank your knowledge of genetics? | | | | | | |
|---|--------------------|---|--|-----------------------------|---------------------------------|---|
| | No Knowledge | Very Poor | Satisfactory | Good | Very Good | |
| Demographic* | 2 (7.7%) | 9 (34.6%) | 11 (42.3%) | 4 (15.4%) | 0 (0%) | |
| Post-Course* | 0 (0%) | 0 (0%) | 7 (26.9%) | 17 (65.4%) | 2 (7.7%) | |
| Post-Workshop | 0 (0%) | 0 (0%) | 6 (26%) | 12 (52.2%) | 5 (21.7%) | |
| Final | 0 (0%) | 0 (0%) | 5 (20%) | 15 (60%) | 5 (20%) | |
| How comfortable do you feel with dealing with genetics issues with your patients? | | | | | | |
| | Very Uncomfortable | Uncomfortable | Neither Comfortable nor Uncomfortable | Comfortable | Very Comfortable | |
| Demographic* | 0 (0%) | 2 (7.7%) | 9 (34.6%) | 14 (53.9%) | 1 (3.9%) | |
| Post-Course* | 0 (0%) | 0 (0%) | 2 (7.7%) | 14 (53.9%) | 10 (38.5%) | |
| Post-Workshop | 1 (4.5%) | 0 (0%) | 1 (4.6%) | 14 (63.6%) | 6 (27.3%) | |
| Final | 2 (8%) | 0 (0%) | 3 (12%) | 13 (52%) | 7 (28%) | |
| How often do you complete a family history for a new patient? | | | | | | |
| | Never | Sometimes | Often | Always | | |
| Demographic | 1 (3.9%) | 5 (19.2%) | 9 (34.6%) | 11 (42.3%) | | |
| Post-Course | 6 (19.2%) | 5 (19.2%) | 7 (26.9%) | 8 (30.8%) | | |
| Post-Workshop | 2 (8.7%) | 7 (30.4%) | 3 (13%) | 11 (47.8%) | | |
| Final | 0 (0%) | 5 (20%) | 6 (24%) | 14 (56%) | | |
| In your practice, how often do you discuss genetics with a patient? | | | | | | |
| | Never | Only if the patient has a genetic condition | Occasionally, but only if there is a good reason | Often, whenever appropriate | Mostly, it is my usual practice | Almost always, with almost all patients |
| Demographic | 1 (3.9%) | 8 (30.8%) | 7 (26.9%) | 5 (19.2%) | 3 (11.5%) | 2 (7.7%) |
| Post-Course | 1 (3.9%) | 10 (38.5%) | 0 (0%) | 7 (26.9%) | 2 (7.7%) | 6 (23.1%) |
| Post-Workshop | 0 (0%) | 8 (34.8%) | 0 (0%) | 5 (21.7%) | 4 (17.4%) | 6 (26.1%) |
| Final | 1 (4%) | 4 (16%) | 3 (12%) | 7 (28%) | 6 (24%) | 4 (16%) |

*denotes statistical significance between responses of two time points, defined as p-value <0.05

4.5.4 Course Evaluation

A course evaluation was administered in the follow-up questionnaires at all three time points. It was composed of seven Likert scale questions that asked participants to consider how this project affected their professional development and the perceived value to both their patients and to themselves.

For all seven statements, participants responded most frequently with Moderately Agree and Strongly Agree. T-tests were performed comparing responses between (1) post-course and post-workshop, (2) post-workshop and final, and (3) post-course and final.

Responses to statement 3, “This training program helped me to communicate basic inheritance patterns to patients,” in the post-workshop questionnaire (n=23, 88.5% response rate) were significantly different from the responses in the final questionnaire (n=25, 96.2% response rate). Comparison of responses between these time points showed a statistically significant difference in average attitudes between post-workshop the final questionnaire with respect to the ability of communicating basic genetic information to patients ($p=0.04$).

A breakdown of these questions examining the proportion of positive responses (Agree or Strongly Agree) is available in Figures 12-18 and complete summary of responses to these questions is available in Table 6, where significance is indicated using an asterisk (*).

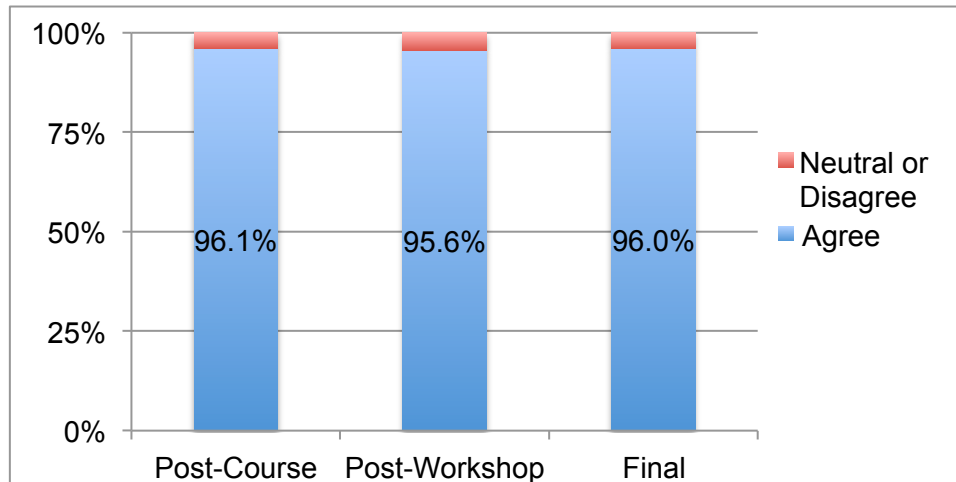


Figure 12. Analysis of attitudes toward This training program advanced my professional development.

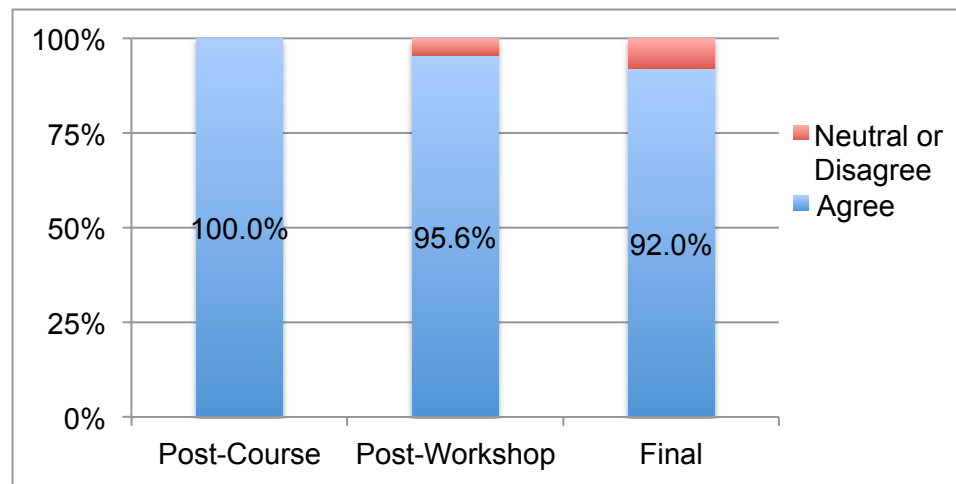


Figure 13. Analysis of attitudes toward This training program increased my knowledge and understanding of genetics.

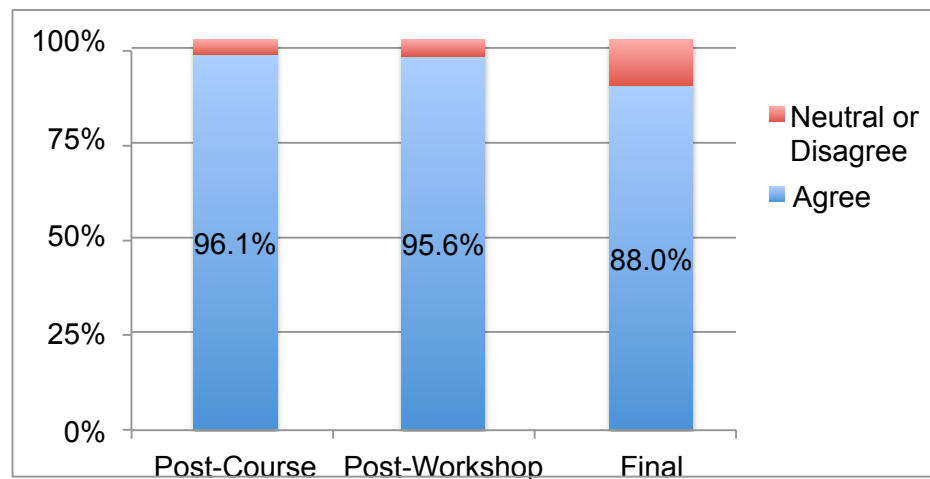


Figure 14. Analysis of attitudes toward This training program helped me to communicate basic inheritance patterns to patients.

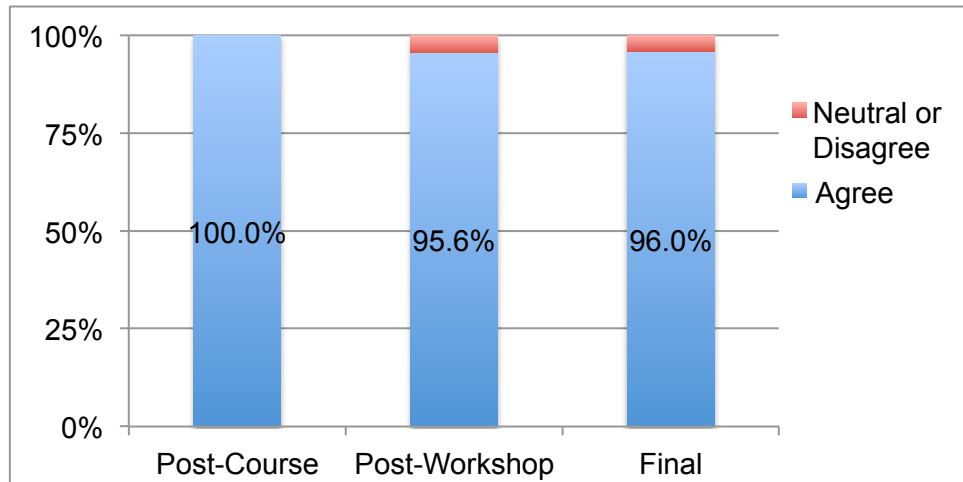


Figure 15. Analysis of attitudes toward I feel confident in my ability to provide basic genetic education to patients.

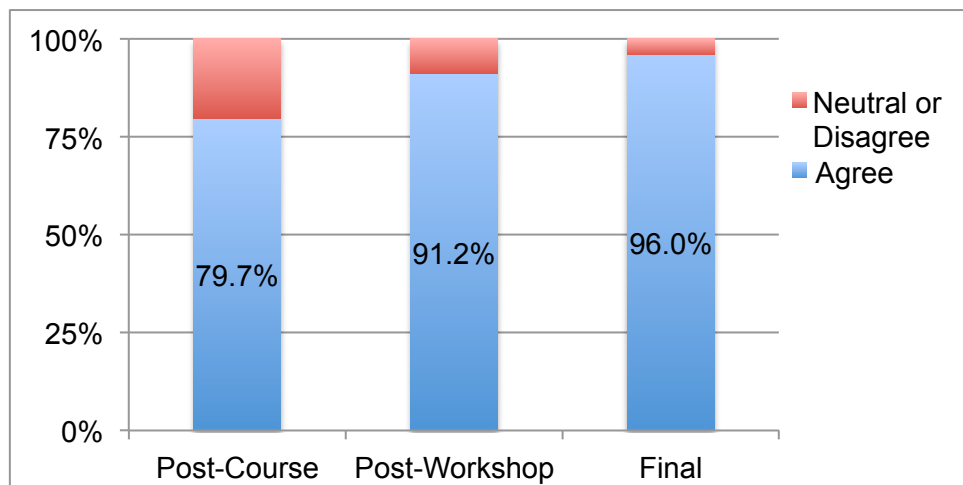


Figure 16. Analysis of attitudes toward Providing patients with basic genetic education fits into the workflow of our clinic.

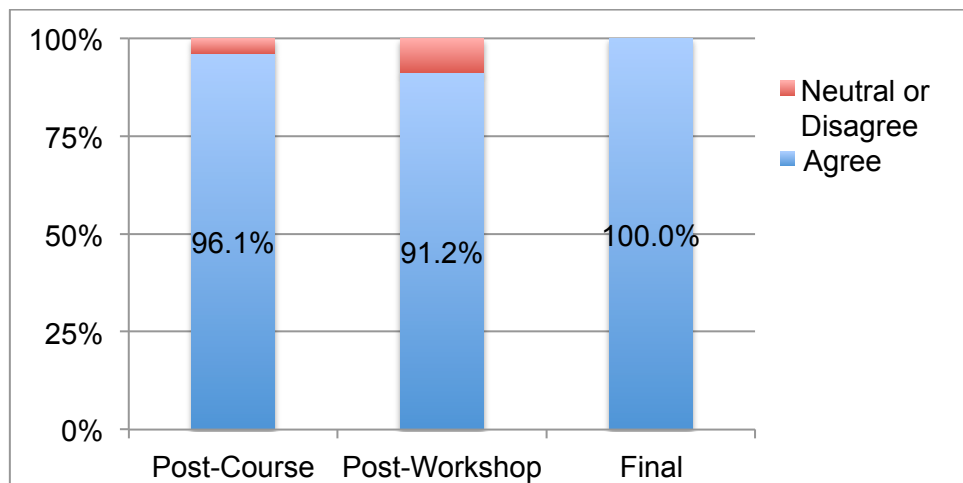


Figure 17. Analysis of attitudes toward Basic genetic education benefits the patients to whom I provide it.

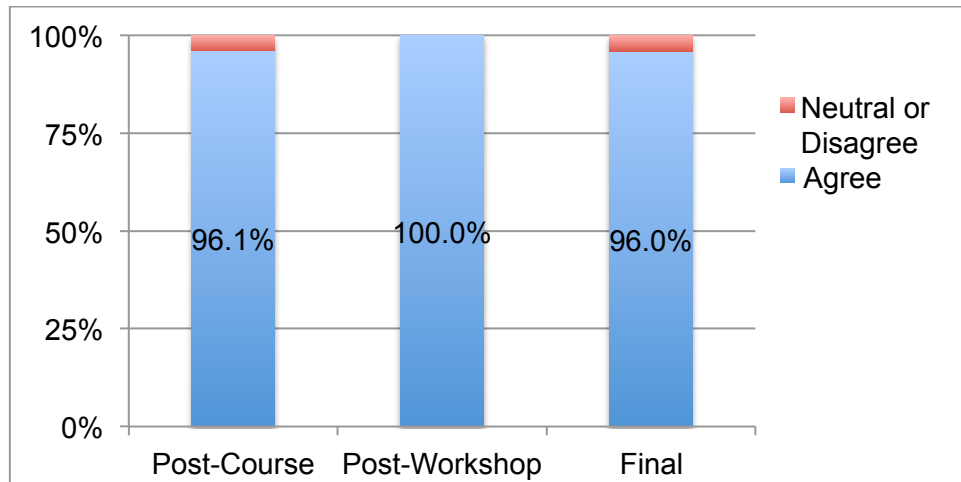


Figure 18. Analysis of attitudes toward It is important to stay current on fundamental information in inherited genetic disease.

Table 6. Course evaluations

| | | | | | |
|---|----------|----------|-----------|------------|------------|
| 1. This training program advanced my professional development. | | | | | |
| | 1 | 2 | 3 | 4 | 5 |
| Post-Course | 0 (0%) | 0 (0%) | 1 (3.9%) | 8 (30.8%) | 17 (65.4%) |
| Post-Workshop | 0 (0%) | 0 (0%) | 1 (4.4%) | 5 (21.7%) | 17 (73.9%) |
| Final | 0 (0%) | 0 (0%) | 1 (4%) | 5 (20%) | 19 (76%) |
| 2. This training program increased my knowledge and understanding of genetics. | | | | | |
| | 1 | 2 | 3 | 4 | 5 |
| Post-Course | 0 (0%) | 0 (0%) | 0 (0%) | 8 (30.8%) | 18 (69.2%) |
| Post-Workshop | 0 (0%) | 0 (0%) | 1 (4.4%) | 3 (13%) | 19 (82.6%) |
| Final | 0 (0%) | 0 (0%) | 2 (8%) | 5 (20%) | 18 (72%) |
| 3. This training program helped me to communicate basic inheritance patterns to patients. | | | | | |
| | 1 | 2 | 3 | 4 | 5 |
| Post-Course | 0 (0%) | 0 (0%) | 1 (3.9%) | 9 (34.6%) | 16 (61.5%) |
| Post-Workshop* | 0 (0%) | 0 (0%) | 1 (4.4%) | 3 (13%) | 19 (82.6%) |
| Final* | 1 (4%) | 0 (0%) | 2 (8%) | 9 (36%) | 13 (52%) |
| 4. I feel confident in my ability to provide basic genetic education to patients. | | | | | |
| | 1 | 2 | 3 | 4 | 5 |
| Post-Course | 0 (0%) | 0 (0%) | 0 (0%) | 10 (30.8%) | 16 (61.5%) |
| Post-Workshop | 0 (0%) | 1 (4.4%) | 0 (0%) | 5 (13%) | 16 (69.6%) |
| Final | 0 (0%) | 0 (0%) | 1 (4%) | 9 (20%) | 15 (60%) |
| 5. Providing patients with basic genetic education fits into the workflow of our clinic. | | | | | |
| | 1 | 2 | 3 | 4 | 5 |
| Post-Course | 0 (0%) | 1 (3.9%) | 4 (15.4%) | 10 (38.5%) | 10 (38.5%) |
| Post-Workshop | 0 (0%) | 1 (4.4%) | 1 (4.4%) | 9 (39.1%) | 12 (52.2%) |
| Final | 0 (0%) | 0 (0%) | 1 (4%) | 12 (48%) | 12 (48%) |
| 6. Basic genetic education benefits the patients to whom I provide it. | | | | | |
| | 1 | 2 | 3 | 4 | 5 |
| Post-Course | 0 (0%) | 0 (0%) | 1 (3.9%) | 12 (46.2%) | 13 (50%) |
| Post-Workshop | 0 (0%) | 1 (4.4%) | 1 (4.4%) | 8 (34.8%) | 13 (56.5%) |
| Final | 0 (0%) | 0 (0%) | 0 (0%) | 10 (40%) | 15 (60%) |
| 7. It is important to stay current on fundamental information on inherited genetic disease | | | | | |
| | 1 | 2 | 3 | 4 | 5 |
| Post-Course | 1 (3.9%) | 0 (0%) | 0 (0%) | 4 (15.4%) | 21 (80.8%) |
| Post-Workshop | 0 (0%) | 0 (0%) | 0 (0%) | 2 (8.7%) | 21 (91.3%) |
| Final | 0 (0%) | 0 (0%) | 1 (4%) | 2 (8%) | 22 (88%) |

*denotes statistical significance between responses of two time points, defined as p-value <0.05

1 = Strongly Disagree, 2 = Moderately Disagree, 3 = Neutral/Don't know, 4 = Moderately Agree, 5 = Strongly Agree

5.0 DISCUSSION

5.1 CONSIDERATION IN PROGRAM DESIGN

This project was designed and implemented at the request of a group of medical professionals interested in having more accessible clinical genetics services within Indian eye clinics. Lack of access to genetic services across India is outlined in existing literature and acts as a needs assessment for such services. Many studies, although small in number and focused on a single disease, have been conducted in locations in many regions of India demonstrating the need for genetic counseling or similar services in areas with limited access. These authors share conclusions of a need for genetic counseling as well as a need for genetic awareness in India based on India being a developing country, high birth rate, low literacy and socioeconomic status, absence of widely available genetic testing, and the existence of molecular laboratories without genetic counseling staff members (Ramprasad, *et al.*, 2007; Mohanty and Das, 2011; Verma, *et al.*, 2012; Kumar, *et al.*, 2012; Muthuswamy, 2011).

In order to ensure the highest cultural awareness and competence possible, an international advisory committee was formed to review and edit all course materials. This was felt to be important because previous studies have demonstrated the diversity of ethnic groups in India as well as risks associated with interventions performed without careful considerations (Mohanty and Das, 2011). Over 4,635 ethnic groups make up the population of India, and thus

many considerations went into the design of this project. A study within tribals of India by Mohanty and Das in 2011 concluded that sophisticated and intricate exploration of psychosocial and cultural aspects considered before implementing counseling in tribals of India (Mohanty and Das, 2011). This statement may be generalized that cultural considerations should be explored before implementing any change in another nation. Without these considerations, projects may carry great risk of adverse events and/or unintended outcomes. Furthermore, The National Society of Genetic Counselors (NSGC), in 2010, informally proposed two ideas to aid in incorporating greater diversity and cultural competence into the field of genetic counseling. One proposed creating a network to share cultural information with applicable counseling strategies that included experiences as they are gained. The other was to develop a standard of multicultural competencies, similar to the NSGC code of ethics that outlines the minimum requirements for cultural competency in education programs (Warren, 2011).

It was decided that this project would be disseminated in an online, modular presentation format as previous studies with pre- and post-test assessments as other studies have shown success in using this type of course for medical students and primary care physicians to increase confidence, comfort, and competency in the subject. This has been done successfully through different delivery models including online programs and in-person workshops (Carroll 2007; Metcalf 2010).

5.2 SPECIFIC AIM 1: EFFICACY OF EDUCATION PROGRAM

A total of 26 individuals took part in the online training course and all participants were able to complete all tasks on time suggesting that the format and timeline were realistic for our study

population. Our hypothesis for Aim 1 was supported in that the online education program showed a statistically significant difference between pre- and post-test knowledge assessment scores for each module. The statistically significant differences in scores between pre- and post-test knowledge assessments are an indication that the educational video modules were a successful method in teaching the information to our study population. The efficacy of this online education program is consistent with a previous study that used a modular online course to teach genetics to medical students. This study also saw a statistically significant difference between pre- and post-test scores for all modules (Metcalf, *et al.*, 2009). These results suggest that Specific Aim 1 was successfully achieved.

5.3 SPECIFIC AIM 2: IMPLEMENTATION

As shown by logbooks maintained by a subset of participating centers, Genetic Educators saw a cumulative total of 497 patients during the implementation period, which is likely an underestimate. Our hypothesis for Aim 2 was supported by the way that sites implemented skills from the education program based on their clinical workflows. For two centers, implementation was initiated but not sustained for reasons to be discussed later. In centers that have routinely implemented genetic education, this project has been of benefit, as described by participants and site supervisors. Therefore, we can conclude that uptake of implementation occurred in 100% of centers, but sustained implementation has occurred in 77.8% of centers. In the 7 out of 9 of centers where implementation has been sustained, a distinct clinical flow pathway had been constructed, with Genetic Educators working in the same clinics as the site supervisors. In the 2 centers where implementation was not sustained, no specific patient flow had been delineated

and the Genetic Educators worked in clinics remote from the site supervisors. We conclude, therefore, that the success of sustained implementation is dependent on a proposed protocol for delivery of genetic education with Genetic Educators working in close proximity, if not the same clinic, as the site supervisor.

Centers that have not been using Genetic Educators formally thus far do note that they are in the process of creating a protocol to implement. Busy clinics and limited personnel are current barriers. Challenges associated with adding genetic service provision duties onto the existing responsibilities of physicians have been reported. In a systematic literature review, Suther and Goodson reveal that the most frequently described barrier is lack of genetic information (2003). However, lack of time was a common barrier among 4 of 18 studies reviewed (Suther and Goodson, 2003).

5.4 DATA EVALUATION

Two questions achieved statistical significance between the demographic questionnaire and post-course follow-up questionnaire. These questions were “How would you rank your knowledge of genetics?” and “How comfortable do you feel with dealing with genetics issues with your patients?” Knowledge and comfort in genetics increased significantly following the online education course as demonstrated by analysis of questionnaire responses. Comparison of responses of these questions between other time points did not yield statistical significance and analysis of all other demographic/follow-up questions was not significant across any of the assessed time points.

Likert scale responses to the statements included in the series of follow-up questionnaires served as course evaluation. Answers closer to 1 (Strongly Disagree) indicated a more negative opinion while answers closer to 5 (Strongly Agree) indicated a more positive opinion. For all statements, the large majority of individuals moderately or strongly agreed while relatively few individuals were neutral or disagreed. This suggests that participants viewed the project positively overall.

5.5 COMMENTS AND OBSERVATIONS

5.5.1 Factors Influencing Degree of Implementation

All centers were asked to implement an in-person service delivery model for genetic education; however, the efficient patient pathways between the participating centers are not identical. This approach was reasonable as in-person service delivery is the most common method of providing genetic counseling services in the United States, despite the unique and individual needs for the included organizations (Cohen et al., 2013).

Following clinical observations, it was clear that degree of implementation varied across participating centers. The exposure to Genetic Educators was greater where (1) a patient pathway was established including designated time and space for genetic education and (2) direct supervision of the Genetic Educator by the site supervisor. There are three main ways in which centers in the current study are utilizing genetic education. The first method utilizes the Genetic Educator on an on-call basis where any physician within the center can refer a patient as necessary. Genetic education can then occur in a dedicated and private space. The second

method designates certain clinic days each week to genetic education patients. The last method integrated responsibilities of genetic education into the pre-existing duties of the Genetic Educator. An example of this included taking a pedigree and providing genetic education during an appointment to obtain imaging or testing. The need for integration of responsibilities has been described in the context of a neurogenetics clinic, a medical specialty with expanding genetics knowledge similar to ophthalmic genetics. It has been suggested that individuals with neurogenetics training (training in both the medical specialty of neurology and in genetics) provide more effective and efficient patient care than having separate neurologists and medical geneticists. (Hanna and Wood, 2002).

Some centers implemented genetic education in a specialized outpatient clinic with a high incidence of genetic disease, such as pediatric glaucoma clinic, pediatric retina clinic, and adult retina clinic. Centers where the Genetic Educator's primary responsibilities were within the clinic where genetic education was introduced also affected the degree of implementation.

In eye clinics where the above two criteria were not met, patient exposure to Genetic Educators was decreased. Other factors that were observed in these centers included Genetic Educators having to leave their main duties to provide genetic education in other clinics or working in a different location. These are barriers to implementation of genetic services within ophthalmic clinics that, to our knowledge, have not been previously described.

5.5.2 Educational Content and Family History Taking

In 45 patient encounters, a 3-generation pedigree was collected in all cases, but genetic concepts were explained in only 8. This discrepancy cannot be easily explained, although lack of time, comfort, and assumed patient understanding are possible barriers; the clinical utility of

explanation of genetic concepts may be less important clinically, and its emphasis in the course should be re-evaluated.

History of miscarriage was directly addressed in only 11 of 45 encounters. Inclusion of miscarriage in health history taking was reviewed in Module 6 of the course due to the associations of miscarriages with chromosomal abnormalities and perinatal lethal conditions. Genetic Educators felt uncomfortable asking about miscarriages but stated that it was not due to any specific cultural aspect. Further education regarding the clinical importance of miscarriages in family history taking may be necessary to better equip Genetic Educators to broach this issue with patients.

In all encounters, ocular histories were asked of family members while gathering pedigree information. However, only 32 encounters elicited extra-ocular history. The differences in diversity of questions provide insight on the way that specific clinics evaluate medical histories to establish diagnoses, management and treatment. Questions to collect information during pedigree taking were often generalized.

5.5.3 Cultural Themes

Cultural themes became apparent during family history taking across participating centers, with the main issue being the subject of consanguinity. The major cultural groups in India, Hindu and Muslim, have strong views on consanguinity and the distribution of these two groups varies based on geographic region. In the Hindu tradition consanguineous marriages are opposed (except in regions of South India, specifically Andhra Pradesh, where LVPEI centers are located) while in Muslim tradition they are common and preferred (Sathyanarayana Rao, *et al.*, 2009). This affected the way in which consanguinity was addressed or not addressed by Genetic

Educators. A striking example of this was in New Delhi, where patients of Hindu origin were not asked about consanguinity for fear of causing offense, while patients of Muslim faith were repeatedly asked for possibility of consanguinity—not only in the parental union, but also in previous generations. In eye clinics serving a large, regional population in which Hindus and Muslims are both represented, the Genetic Educators used cultural indications such as name and appearance to determine which group a patient belonged.

In southern India, consanguinity rates reach as high as 36.5% in the state of Andhra Pradesh, where most of the LVPEI centers are located (Bittles and Black, 2013). Due of this, some Genetic Educators based in these regions misinterpreted the purpose of taking a pedigree as being related to the high rate of consanguinity. Here, the Muslim population was in the majority so consanguinity was often assumed. Consanguinity was asked about in session to identify potentially multiple consanguineous marriages within a family. In summary, one important point to consider when implementing genetic education across India, is the importance of promoting distance from cultural stereotypes as they may limit patient care. It was stressed that it is important to address consanguinity with every patient, regardless of cultural norms.

5.5.4 Adverse Events

Site supervisors were asked to inform us of any adverse events as a direct result of genetic education. As part of the observational period, all supervisors were asked directly about the occurrence about adverse events and none were reported.

Anecdotally, people have had reservations about doing such interventions because of the risk for adverse events. This is the first study to our knowledge that has used informal interview to document the presence or absence of adverse events as a result of the implementation of

genetics education. The absence of adverse events in this study suggests that interventions can be successful if proper precautions are considered.

5.5.5 Feedback from Genetic Educators and Site Supervisors

During the second field trip, informal interview allowed for feedback from Genetic Educators and site supervisors. Their comments can generally be categorized into positive impact of the project, barriers, and implications for the future.

Many positive comments were received regarding the impact of the current study. The most frequent comment shared between participating centers is that implementation of this program increased the throughput and efficiency of clinics. Other comments mentioned increasing awareness of genetics not only among other staff members, but also increasing awareness of genetics among patients. This is a shared goal of other similar clinics. At the Ocular Genetics Program within the Hospital for Sick Children in Toronto, Ontario of Canada, one of the main program goals is to increase patient knowledge of genetics (Morad, *et al.*, 2007).

In addition to conclusions drawn from data, participants and supervisors also verbalized some perceived barriers to extent and consistency of implementation. These included interrupting heavy clinical flow and discomfort broaching potentially uncomfortable topics with patients.

In terms of implications for the future, this is two-fold. First, the project has generated an interest in multiple participants to continuing education in genetic counseling or medical genetics. Interest from the medical community in genetics and genetic counseling is an important step in initiating clinical genetics services. In the United Kingdom, genetics services in a primary care setting have been able to be provided by nurses with a specific interest in genetics

(Westwood, *et al.*, 2006). Second, a supervisor feels that this pilot study is an early step in justifying the need for wider development of ophthalmic genetics in India.

5.6 FUTURE STUDIES

Due to the documented improvements in genetic education of paramedical health staff participating in this pilot study, the 100% implementation rate of genetic education and the perceived improvement in patient care, it is clear that a similar course could be repeated. When repeated, the course should focus less on molecular genetics and more on clinical applications. The in depth background information was not necessary for the way in which genetic education was implemented through the current project. Resources can be provided to any individual interested in learning that information.

Since the most widely implemented skill has been pedigree-taking, the new course should increase emphasis on this, including more complicated cases. Additional focus should be placed on more detailed medical history taking including symptom-based questions of both ocular and systemic features. Participants have also expressed desire to learn more strategies in explaining why pedigrees or genetic education is of benefit to a patient as well as strategies to ask about uncomfortable topics like miscarriages and consanguinity. More emphasis must also be placed on the role of the Genetic Educator, outlining what is within their responsibilities and what has to be deferred to physicians.

The accuracy of pedigrees obtained during the implementation period was not analyzed. This accuracy would be defined as use of standard pedigree conventions as detailed by Bennett, *et al* (1995). Our group plans to obtain a number of pedigrees from each participant for analysis

by an independent observer. This study would serve as an indirect measure of the ability of present study to effectively teach standardized pedigree notation.

When asked directly, a site supervisor expressed interest in the potential for this course to be offered in person, rather than online. Another supervisor suggested included providing incentive for participants, as some had to cover the cost of travel to the workshop out-of-pocket. Genetic Educator duties often did not replace but were added onto pre-existing clinic responsibilities; compensation was suggested as a motivating factor.

There is a current plan to repeat the course in India before launching programs in other countries. Repeating the course in India will allow participation of other centers as well as pilot centers to train additional individuals. It is important that the study be replicated with success within the same nation before altering the course to accommodate other cultures or medical subspecialties.

There is also interest in the creation of a course for site supervisors and physicians in pedigree interpretation. Many physicians are not absolutely confident in their ability to analyze complex pedigrees. It is felt that a course that details complex analysis would help these selected eye clinics utilize pedigrees in patient care. Concepts that could be covered include variable expressivity, penetrance, age of onset, anticipation, sex-limited traits, skewed X inactivation, gonadal mosaicism, *de novo* mutations, regions of homozygosity, and founder effect. Other programs in the United States have provided similar education to physician's assistants, nutritionists, dentists, and other medical groups as continuing education as clinical genetics services have become more prevalent in medicine (NCHPEG, 2014). This shows that there is a need for such education in both developed and developing countries.

5.7 CONCLUSION

Overall, this pilot study was successful in introducing a clinical service that was not previously offered or uniformly available in the participating institutes. The education course was effective in teaching participants the information contained in the seven course modules, as shown by statistically significant improvements in test scores from pre-tests to post-tests. Implementation has been ongoing for over six months and there have been no adverse events reported from patients or colleagues, which provides support that this service can be provided safely. The majority of centers have implemented the pedigree aspect of this course rather than the explanation of genetics concepts. This was dependent on workflow of the clinic and the confidence of the Genetic Educator. Of note, all participants are able to construct at least 3-generation pedigrees through conversation with patients. It is clear that for successful, sustained implementation, the following are necessary: (1) an established patient pathway with designated space and/or time for genetic education, and (2) direct supervision of the Genetic Educator by the site supervisor. At every stage of this course, it was apparent that the Genetic Educators did not attempt counseling and understand the gravity of inappropriate counseling interactions. The overall opinion of the course, as gathered by evaluations and informal interviews, is positive. It appears the greatest perceived benefit to physicians is the increased efficiency of clinic, demonstrated by the number of pedigrees obtained and less professional time spent detailing patient histories. The goal of this project was met in that the results show that an online course was sufficient to teach paramedical and health professionals to provide basic genetic services in a manner that is safe and of perceived benefit to clinical flow and patient care.

APPENDIX A

UNIVERSITY OF PITTSBURGH INSTITUTIONAL REVIEW BOARD APPROVAL



University of Pittsburgh *Institutional Review Board*

3500 Fifth Avenue
Pittsburgh, PA 15213
(412) 383-1480
(412) 383-1508 (fax)
<http://www.irb.pitt.edu>

Memorandum

To: Dr. Kanwal Nischal
From: Sue Beers, Ph.D., Vice Chair
Date: 3/26/2013
IRB#: [PRO13020479](#)
Subject: Providing basic genetics education to paramedical/health professionals at selected Indian ophthalmic centers

The above-referenced project has been reviewed by the Institutional Review Board. Based on the information provided, this project meets all the necessary criteria for an exemption, and is hereby designated as "exempt" under section 45 CFR 46.101(b)(1) Educational strategies, curricula or classroom management methods.

Please note the following information:

- If any modifications are made to this project, use the "**Send Comments to IRB Staff**" process from the project workspace to request a review to ensure it continues to meet the exempt category.
- Upon completion of your project, be sure to finalize the project by submitting a "**Study Completed**" report from the project workspace.

Please be advised that your research study may be audited periodically by the University of Pittsburgh Research Conduct and Compliance Office.

APPENDIX B

ETHICS BOARD/PERMISSION LETTERS FROM INDIA SITES



University of Pittsburgh
Graduate School of Public Health
Department of Human Genetics

Date: 1. MARCH 2013.

LETTER OF PERMISSION

I, PROF. R.V. AZAD., hereby give permission to the University of Pittsburgh to conduct the study "Providing basic genetic education to paramedical/health professionals at selected Indian ophthalmic centers" with employees of my center. I also give permission to the study staff to personally visit my center as outlined in the project methods. Any specific visitor policies will be made available to the study staff.

I have read the description of the project in its entirety and believe that the study staff is taking the necessary steps to ensure that its execution is culturally competent and appropriate for taking place in India.

Check one below:

☒ The IRB or Ethics Committee of my center has been consulted on this project and **DOES NOT** require review in order for our employees to participate.

☐ The IRB or Ethics Committee of my center has been consulted on this project and **DOES** require review in order for our employees to participate.

Signature: _____

(Site supervisor representing the below center)

Center: _____

Dr R P Centre AIIMS

PROF. RAJVARDHAN AZAD
CHIEF
Dr. R.P. Centre for Ophthalmic Sciences
AIIMS, New Delhi-110029



University of Pittsburgh
Graduate School of Public Health
Department of Human Genetics

Date: 7th March 2013

LETTER OF PERMISSION

I, Dr. A.S. KARTHIGEYAN, hereby give permission to the University of Pittsburgh to conduct the study "Providing basic genetic education to paramedical/health professionals at selected Indian ophthalmic centers" with employees of my center. I also give permission to the study staff to personally visit my center as outlined in the project methods. Any specific visitor policies will be made available to the study staff.

I have read the description of the project in its entirety and believe that the study staff is taking the necessary steps to ensure that its execution is culturally competent and appropriate for taking place in India.

Check one below:

☒ The IRB or Ethics Committee of my center has been consulted on this project and **DOES NOT** require review in order for our employees to participate.

☐ The IRB or Ethics Committee of my center has been consulted on this project and **DOES** require review in order for our employees to participate.

Signature: _____



(Site supervisor representing the below center)

Center: _____

ARAVIND EYE HOSPITAL, MADURAI



University of Pittsburgh
Graduate School of Public Health
Department of Human Genetics

Date: 2-3-2013

LETTER OF PERMISSION

I, Ramesh Kekunnaya, hereby give permission to the University of Pittsburgh to conduct the study "Providing basic genetic education to paramedical/health professionals at selected Indian ophthalmic centers" with employees of my center. I also give permission to the study staff to personally visit my center as outlined in the project methods. Any specific visitor policies will be made available to the study staff.

I have read the description of the project in its entirety and believe that the study staff is taking the necessary steps to ensure that its execution is culturally competent and appropriate for taking place in India.

Check one below:

☒ The IRB or Ethics Committee of my center has been consulted on this project and **DOES NOT require review** in order for our employees to participate.

☐ The IRB or Ethics Committee of my center has been consulted on this project and **DOES require review** in order for our employees to participate.

Signature: _____

(Site supervisor representing the below center)

Center: _____

L.V. Prasad Eye Institute, HYDERABAD, INDIA



University of Pittsburgh
Graduate School of Public Health
Department of Human Genetics

Date: 5 March 2013

LETTER OF PERMISSION


I, Prof G Kumaramanickavel, hereby give permission to the University of Pittsburgh to conduct the study "Providing basic genetic education to paramedical/health professionals at selected Indian ophthalmic centers" with employees of my center. I also give permission to the study staff to personally visit my center as outlined in the project methods. Any specific visitor policies will be made available to the study staff.

I have read the description of the project in its entirety and believe that the study staff is taking the necessary steps to ensure that its execution is culturally competent and appropriate for taking place in India.

Check one below:

☒ The IRB or Ethics Committee of my center has been consulted on this project and **DOES NOT require review** in order for our employees to participate.

☐ The IRB or Ethics Committee of my center has been consulted on this project and **DOES require review** in order for our employees to participate.

Signature: 
(Site supervisor representing the below center)

Center: Narayana Nethralaya, Bangalore and Aditya Jyot Hospital, Mumabi, India.



University of Pittsburgh
Graduate School of Public Health
Department of Human Genetics

Date: 21/03/2013

LETTER OF PERMISSION

I, Dr. Lushmi Kaurshik, hereby give permission to the University of Pittsburgh to conduct the study "Providing basic genetic education to paramedical/health professionals at selected Indian ophthalmic centers" with employees of my center. I also give permission to the study staff to personally visit my center as outlined in the project methods. Any specific visitor policies will be made available to the study staff.

I have read the description of the project in its entirety and believe that the study staff is taking the necessary steps to ensure that its execution is culturally competent and appropriate for taking place in India.

Check one below:

☒ The IRB or Ethics Committee of my center has been consulted on this project and **DOES NOT require review** in order for our employees to participate.

☐ The IRB or Ethics Committee of my center has been consulted on this project and **DOES require review** in order for our employees to participate.

Signature: _____

(Site supervisor representing the below center)

Center: _____

Postgraduate Institute of Medical Education & Research,
Chandigarh, India.



University of Pittsburgh
Graduate School of Public Health
Department of Human Genetics

Date: 4th March 2013

LETTER OF PERMISSION

I, **Dr. Suma Ganesh**, hereby give permission to the University of Pittsburgh to conduct the study "Providing basic genetic education to paramedical/health professionals at selected Indian ophthalmic centers" with employees of my center. I also give permission to the study staff to personally visit my center as outlined in the project methods. Any specific visitor policies will be made available to the study staff.

I have read the description of the project in its entirety and believe that the study staff is taking the necessary steps to ensure that its execution is culturally competent and appropriate for taking place in India.

Check one below:

√ The IRB or Ethics Committee of my center has been consulted on this project and **DOES NOT require review** in order for our employees to participate.

 The IRB or Ethics Committee of my center has been consulted on this project and **DOES require review** in order for our employees to participate.

Signature:

(Site supervisor representing the below center)

Center: **Dr. Shroff's Charity Eye Hospital**

APPENDIX C

SCRIPT FOR PARTICIPANTS

Dear Course Participant,

This genetics course is part of a research study that assesses the effectiveness of an online program to teach paramedical/health professionals about basic genetics and inherited ophthalmic conditions. We plan to use three types of questionnaires, which will be administered throughout the 7-week course.


If you are willing to participate, this first questionnaire will ask you about your work environment and responsibilities. At the beginning of each weekly module, you will be asked to complete a knowledge assessment. This allows us to measure your baseline knowledge of the information that is about to be presented. We do not expect you to answer all of the questions correctly and no grade or score will be provided. After completing the week's module, you will be asked to complete another knowledge assessment. After this assessment, you will receive a test score and feedback about each of your answers will be provided. After the course, you will be asked to rank the 3 lectures you found most challenging and to complete a follow-up questionnaire.

Shortly after the conclusion of the online course, some of the course administrators will travel from Pittsburgh to India. You will have the opportunity to discuss the course material in detail prior to applying the content to your job responsibilities in your workplace.


You may benefit from participating by gaining knowledge and skills that expand the services of your clinical practice. There are no foreseeable risks associated with this project. Your confidentiality will be maintained by a unique login ID that will allow you to access the course and questionnaires. You will not receive payment for participating. Participation is voluntary and you may withdraw from the project at any time. This study is being conducted by Dr. Ken K. Nischal, a pediatric ophthalmologist, and Holly Babcock of the University of Pittsburgh, who can be contacted at heb36@pitt.edu with any questions.

APPENDIX D

MODULE SLIDES




Children's
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GENETIC EDUCATOR TRAINING COURSE



University of Pittsburgh Graduate School of Public Health



World Society of Paediatric Ophthalmology and Strabismus

MODULE 1:

MOLECULAR BIOLOGY

Module 1

Purpose:
To provide a foundation of basic molecular biology concepts

Objectives:
Upon completing this module, participants should be able to:

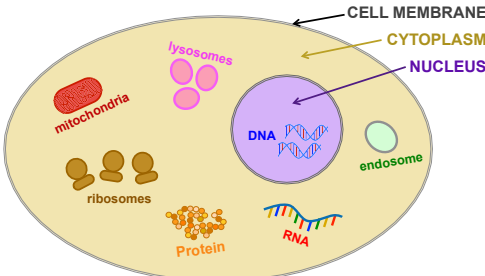
1. Identify the functions of DNA, RNA, and Protein
2. Compare and contrast DNA and RNA
3. Explain the Central Dogma of Molecular Biology

Basic Molecules of Life

- All living things are made up cells containing basic organic molecules
- Some of the most important organic molecules are:
 - Nucleic Acids (DNA and RNA)
 - Proteins
- This module will focus on these molecules, as they relate to human genetics

Human Cell Diagram

This drawing is an example of some of the parts found in one human cell. You can imagine that each part is floating around in the cell, contained in either the nucleus or cytoplasm.



Labels in diagram: CELL MEMBRANE, CYTOPLASM, NUCLEUS, lysosomes, mitochondria, ribosomes, Protein, RNA, endosome, DNA.

Introduction to the Central Dogma

- DNA, RNA, and Protein are the 3 components of the theory called “**The Central Dogma**”
- The Central Dogma refers to the **cellular flow of information** which reads our genetic material and converts it to functional molecules
- In order for the genetic information in our DNA to be useful, it has to be converted into different molecules (mRNA and protein) through this process, The Central Dogma

Introduction to the Central Dogma

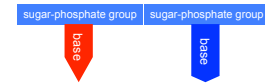
- The Central Dogma flow of information is:

DNA → RNA → Protein

- We will build on this important concept throughout this module and discuss each of the 3 components in detail

Nucleic Acids – Introduction

- Nucleic acids include: DNA and RNA
- All nucleic acids are composed of **nucleotides**
- Each nucleotide consists of:
 - 1 Sugar-phosphate group
 - 1 Base
 - DNA bases: A, C, G, T
 - RNA bases: A, C, G, U



Nucleic Acids

- We will begin discussing the 1st part of the Central Dogma:

DNA

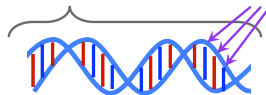
Nucleic Acids – DNA

DNA → RNA → Protein

- DNA** stands for **d**eoxyribo**n**ucleic **a**cid
- DNA is an individual's **source of genetic information** that tells the body how to grow and develop
- DNA is packaged into genes, which are further packaged into chromosomes. These concepts will be discussed more in Module 2.

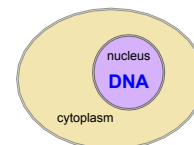
DNA (Building Blocks)

- DNA is a larger molecule built from single units
- Single units of **DNA** are called **NUCLEOTIDES**



Nucleic Acids – DNA

- Location in human cell: Nucleus**



- Structure:** Double-stranded and then twisted into a "double helix"



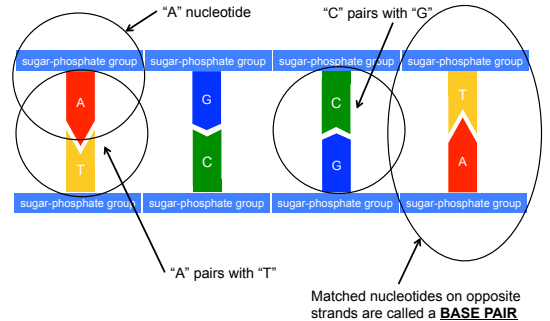
DNA (nucleotides)

- **DNA** consists of nucleotides with bases **A, C, G, and T**
- These letters represent the 4 DNA nucleotides that make up a DNA sequence. The letters stand for:

A = Adenine C = Cytosine
G = Guanine T = Thymidine

- Each of DNA's double strands has a nucleotide sequence and the two strands are connected by hydrogen bonds between bases.
- Each DNA nucleotide should always pair with its complement.
 - **A always pairs with T** and vice versa
 - **C always pairs with G** and vice versa

DNA (double-stranded structure)

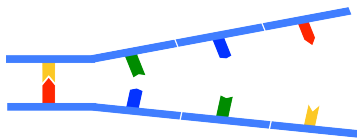


Transcription (DNA → RNA)

- The first arrow in the Central Dogma represents the process of **transcription** which reads information on DNA to create RNA

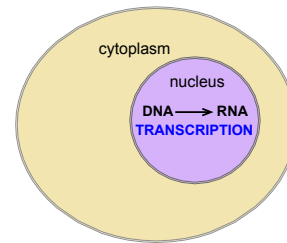
DNA $\xrightarrow{\text{transcription}}$ RNA \longrightarrow protein

- During transcription, the 2 strands of DNA are unzipped and one strand is used as a template to make RNA



Transcription (DNA → RNA)

- In human cells, the process of **transcription** takes place in the **nucleus**



Nucleic Acids – RNA

DNA → RNA → Protein

- **RNA** stands for **ribonucleic acid** and is made during the nuclear process of transcription

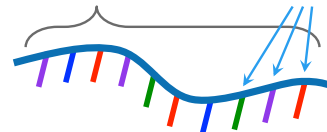
- RNA is also built from 4 nucleotides

A = Adenine C = Cytosine same as DNA
G = Guanine U = Uracil unique to RNA

- There are three (3) major types of RNA:
 - **Messenger RNA (mRNA)**
 - **Transfer RNA (tRNA)**
 - **Ribosomal RNA (rRNA)**

RNA (Building Blocks)

- RNA is also a larger molecule built from single units
- Single units of **RNA** are also called **NUCLEOTIDES**

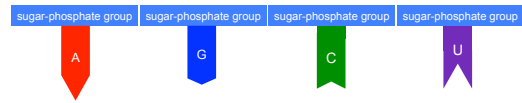


Nucleic Acids – RNA

- As mentioned, there are 3 major types of RNA, but in this module we will focus our attention on:
messenger RNA (mRNA)
- mRNA molecules are created in the nucleus but move into the cytoplasm
- The job of mRNA is to act as an intermediate molecule that carries the genetic code of DNA into the cytoplasm to be made into proteins

mRNA

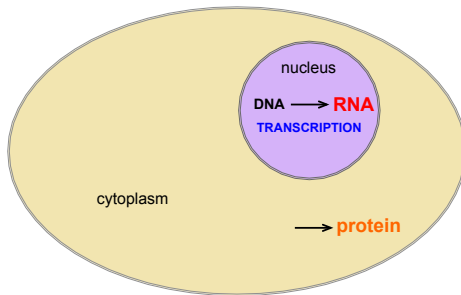
- Structure:** Single-stranded



- The sequence of nucleotides in a strand of mRNA determines the protein that will be created. Thus, different sequences of mRNA are used to make different proteins.

mRNA

mRNA is made in the nucleus and carries the genetic code into the cytoplasm where proteins are created.



Translation (RNA → protein)

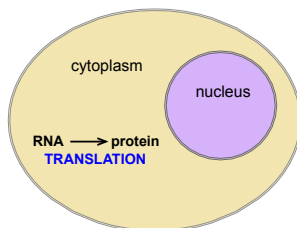
- The second arrow in the Central Dogma represents the process of **translation** which reads information from mRNA to create protein



- mRNA sequence codes for amino acids which are strung together to make proteins

Translation (RNA → protein)

- In human cells, the process of **translation** takes place in the **cytoplasm**

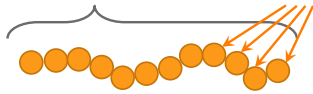


Proteins

- Proteins are created after the cytoplasmic process of translation
- Proteins are built from **amino acids** linked together in different combinations and lengths
- Proteins are the functional molecules that do most of the jobs of the cell including:
 - Structure, transport, repairs, reactions

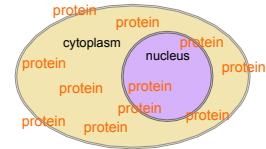
Protein (Building Blocks)

- Proteins are also larger molecules built from single units
- Single units of **protein** are called **AMINO ACIDS**



Proteins

- Location in human cell: **Everywhere**

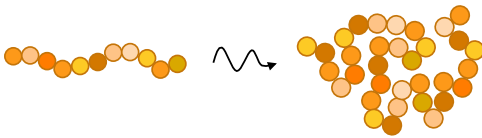


- Primary Structure: String of "beads"
(beads are amino acids)



Proteins

- After translation, proteins look like a string of beads
- They **must** then be specially **folded** in order to function



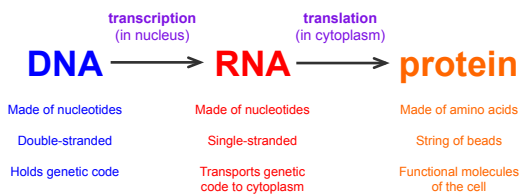
Proteins

- In summary, for proteins to function properly, they must:
 - Be translated from mRNA
 - Have the correct sequence of amino acids
 - Be folded correctly



Central Dogma Summary


- Below is what has been covered regarding the Central Dogma:



Module 1 complete!


- Please take the Module 1 Knowledge Test





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MODULE 2:

CELL CYCLE & GENETICS

Module 2

Purpose:
To provide a context for molecular biology in human genetics and reproduction

Objectives:
Upon completing this module, participants should be able to:

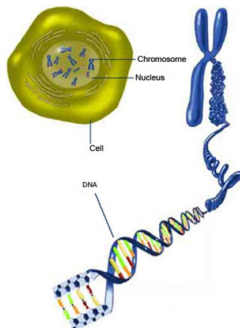
1. Describe the relationship between genetic structures and their functions
2. Describe the human genome and its chromosomes
3. Compare and contrast mitosis and meiosis

Introduction to Genetics

Genetics is the study of inherited differences found in and between human populations and individuals

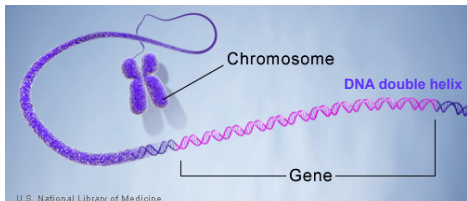
Packaging of Genetic Information

- Each cell in our body contains the same DNA
- The amount of DNA in each cell is very large
 - The long double strands of DNA must be condensed and packaged so that it all fits within the nucleus



Packaging of Genetic Information

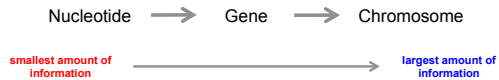
- The strands of DNA are coiled up into structures called **chromosomes**, which contain a massive amount of genetic information
 - **Genes** are made up of DNA
 - **Chromosomes** are made up of many lined up genes



U.S. National Library of Medicine

Packaging of Genetic Information

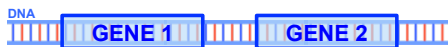
- Let's consider the amount of genetic information contained in each structure
- The order of genetic organization is below:



Genes

- As introduced before, a gene is a section of DNA made of many nucleotides
- Genes are the pieces of DNA that go through the **Central Dogma** to become functional proteins
- A gene is like a single instruction for the body
- Each gene makes a different protein

Genes



- From the image above:
- GENE 1 will make PROTEIN 1

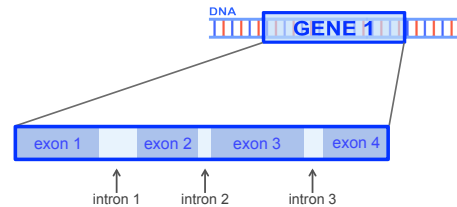


- GENE 2 will make PROTEIN 2



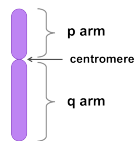
Genes

- Genes are even further divided into two types of regions:
- Exons** – regions that code for proteins
- Introns** – regions that separate exons and do not code for proteins



Chromosome Structure

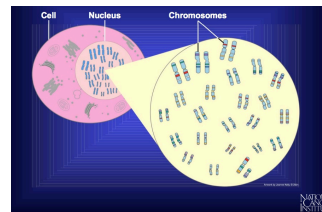
- Many genes on a long strand of DNA coil up to make one chromosome, which looks something like the picture below



- The top and bottom segments are called the two “**arms**”
- The **short arm** is also called the “**p arm**” (named for being “petite”)
- The **long arm** is also called the “**q arm**”
- The arms connect at the “**centromere**” which resembles the “waist” of the chromosome

Chromosomes

- Each human being typically has **23 pairs of chromosomes** (46 total chromosomes) in the nucleus of every cell in the body



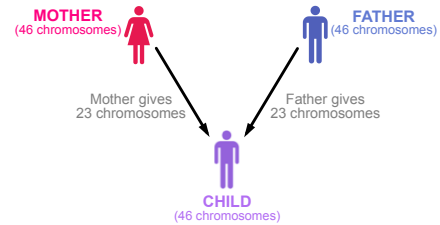
Having 2 copies of each chromosome means that we have 2 copies of every gene!

Human Genome

- All of the genes on all 46 chromosomes together make up the **human genome**
- The human genome contains about 20,000 genes in total

Human Chromosomes

- Chromosomes come in pairs because one comes from the mother and one from the father
- Therefore, individuals have half of their mother's and half of their father's genes, explaining why children resemble both mom and dad



Germline Cells – Egg and Sperm

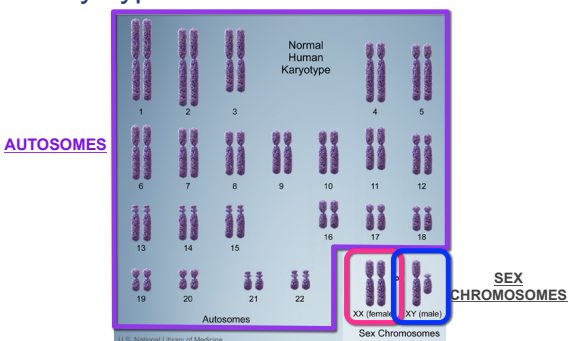
- There is one exception to every cell in the body having 46 chromosomes: germline cells (egg and sperm)
- Egg and sperm contain **23 chromosomes** each
- **Egg and sperm cells** contain **one** of each paired chromosome (23 chromosomes total) so that when they join at conception, the baby has the correct number (46 total: 23 from the mother and 23 from the father)
- Egg and sperm are created in a process called **meiosis**, which we will discuss later in this module



Karyotype

- A **karyotype** is a picture of a single cell's chromosomes
- The chromosomes are shown as 23 pairs, which are numbered according to size (largest to smallest)
- The first 22 pairs of chromosomes (numbered 1 to 22) are called **autosomes**, which are the same in males and females
- The last pair of chromosomes is the **sex chromosomes** (X and Y) and determines whether a person is male or female
 - **Females** have **2 X chromosomes**
 - **Males** have **1 X and 1 Y chromosome**

Karyotype



Karyotype Nomenclature

- If a karyotype is made for an individual, there is a special method to tell us which chromosomes are present, absent or rearranged
- A **normal female** karyotype with all chromosomes present:

46,XX

(tells us there are 46 chromosomes and the sex chromosomes are XX for female)
- A **normal male** karyotype with all chromosomes present:

46,XY

(tells us there are 46 chromosomes and the sex chromosomes are XY for male)

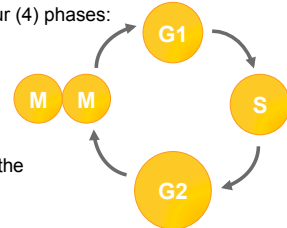
These two notations: **46,XX** and **46,XY** indicate that **no abnormalities were found**

The Cell Cycle

- The cell cycle is how our body creates new cells
- All cells come from existing cells through cell division
- All new cells must have the correct amount of genetic material:
 - 46 chromosomes for most cells
 - 23 chromosomes for egg or sperm

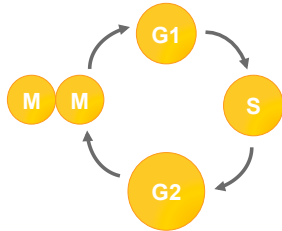
The Cell Cycle

- For a cell to divide and form a new cell, it must grow, double its genetic material, and then split into two cells which are exact copies of the original cell
- The cell cycle has four (4) phases:
 - G1 Phase
 - S Phase
 - G2 Phase
 - M Phase
- The phases occur in the above order



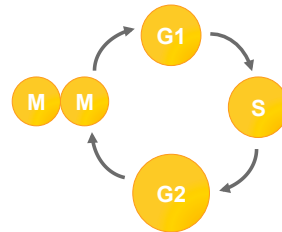
The Cell Cycle – G Phases

- The “G” in **G1** and **G2 phase** stands for “**GROWTH**”
 - The cell needs to become large enough to split into 2 functional cells



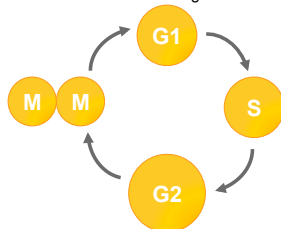
The Cell Cycle – S Phase

- **S Phase** stands for “**SYNTHESIS**”
 - The cell must double its genetic material to have enough for 2 cells
 - New DNA is made or synthesized by DNA Replication



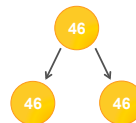
The Cell Cycle

- There are two kinds of **M Phase** depending on what type of cell is being made
 - **Mitosis**: creates cells with same amount of genetic information
 - **Meiosis**: creates cells with half the genetic information (egg/sperm)



MITOSIS

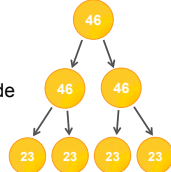
- The cell has doubled its amount of DNA in S phase
- Splits into 2 identical cells with the **SAME DNA as the original cell**
- This is how **MOST** cell division occurs



MEIOSIS

- The cell has doubled its amount of DNA in S phase
- Splits into 2 identical cells with the same DNA as the original cell
- Each cell goes through the cell cycle a **SECOND TIME** but skips the 2nd S phase (DNA does not double)
- Second cell division results in 4 cells with **HALF the original DNA**

- This is how **EGG and SPERM** are made



Mitosis vs. Meiosis

Mitosis

- New cells have **identical** genetic material of original cell
- New cells have 46 chromosomes
- One cell division
- Creates most new cells in the body

Meiosis

- New cells have **half** the genetic material of original cell
- New cells have 23 chromosomes
- Two cell divisions
- Creates egg and sperm

Module 2 complete!

- Please take the Module 2 Knowledge Test



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MODULE 3: INHERITANCE

Module 3

Purpose:

To illustrate the various inheritance patterns and etiologies of ophthalmic disease

Objectives:

Upon completing this module, participants should be able to:

1. Identify various underlying etiologies of ophthalmic disease
2. Describe the characteristics and recurrence risks for Mendelian traits and diseases
3. Describe factors that may mask or alter possible inheritance patterns

Introduction to Inheritance

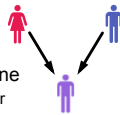
Inheritance is the passing of genetic information from parent to child

Introduction to Inheritance

In this module, we will refer to a **genetic condition** as a condition, disease, or pattern of symptoms that run in families and therefore can be seen in multiple family members

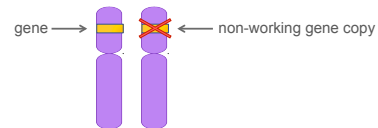
Alleles

- Remember that we have 2 copies of every gene
 - 1 copy on the chromosome inherited from the mother
 - 1 copy on the chromosome inherited from the father
- There can be different forms of the same gene
- The different forms are called **alleles**
- For example, the gene that determines **blood type** has three alleles: **A, B, and O**
 - Each individual gets one allele from each parent
 - The combination of two alleles determine blood type
 - If you receive alleles **A and A**, you are blood type A



Cause of Genetic Conditions

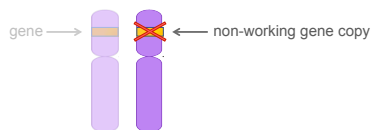
- Genetic conditions result from a **change in a gene** (in one or both copies) that causes it to not work properly



- This change may occur in one or both gene copies
- The way genetic conditions and their symptoms are inherited depend on how many gene copies are affected

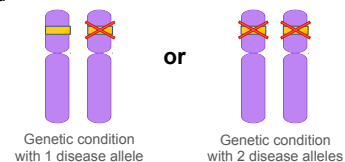
Cause of Genetic Conditions

- The **change** in a gene that causes it to not work may be a:
 - Mutation** (a change in the DNA sequence)
 - Deletion** (missing pieces of the DNA sequence)
 - Duplication** (extra regions of the DNA sequence)



Cause of Genetic Conditions

- The non-working gene copy can be referred to as a "disease allele"
- Some genetic conditions require one disease allele and others require two disease alleles for an individual to be affected

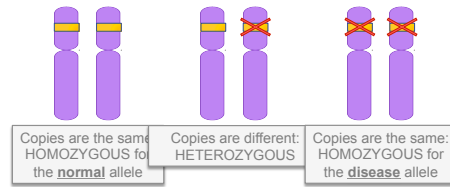


Genotype

- The combination of alleles you have for a certain gene is called your genotype
- The genotype is **homozygous** if the copies are the same
- The genotype is **heterozygous** if the copies are different

The words **homozygotes** and **heterozygotes** refer to people that have the corresponding gene copy combinations

Genotype



Phenotype

- We will define phenotype as the way a particular genotype is expressed in an individual, what you see as the symptoms
- Does the individual show symptoms and which symptoms are present?
- In this module, phenotype will be either:
 - Affected (individual has a disease)
 - Unaffected (individual is free of a disease)

Mendelian Inheritance

- Mendelian inheritance refers to traits, characteristics, or diseases that are caused by a change in **one single gene**
- We will discuss 3 patterns of Mendelian inheritance:
 - Autosomal Dominant**
 - Autosomal Recessive**
 - X-Linked Recessive**

Autosomal Dominant Inheritance

- Autosomal dominant is a Mendelian inheritance pattern where **ONLY ONE** disease allele is required to cause a disease

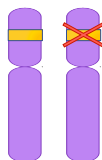
Let's break down the meaning of the term

AUTOSOMAL

- The gene change occurs on an autosome chromosome (1 to 22)
- Equally expressed in males and females

DOMINANT

- The disease can be passed from one generation to the next generation within a family

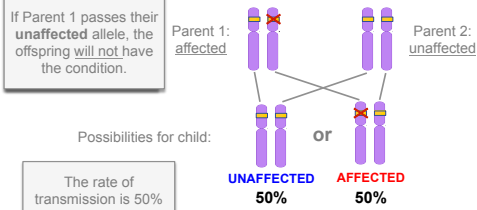


Autosomal Dominant Inheritance

- Heterozygotes are affected**
 - "Dominant" implies that one copy of the affected gene is enough to express the symptoms of a condition
- Individuals with an autosomal dominant disorder typically have **one affected parent**
- Autosomal disorders show a high level of **variability**
 - Variability* means that people in the same family with the same disorder may show different disease symptoms and different severity of disease

Autosomal Dominant Inheritance

- A person with an autosomal dominant disorder has a **50% chance** of passing the condition onto a child



Autosomal Recessive Inheritance

- Autosomal recessive is a Mendelian inheritance pattern where **TWO** disease alleles are required to cause disease

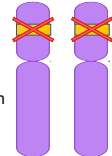
Let's break down the meaning of the term

AUTOSOMAL

- The gene change occurs on an autosome chromosome (1 to 22)
- Equally expressed in males and females

RECESSIVE

- The disease may be hidden in some family generations as carriers do not express the condition
- Family history is usually negative for the disease

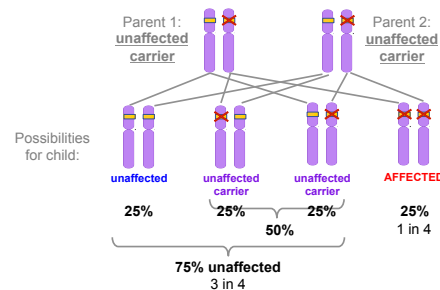


Autosomal Recessive Inheritance

- Heterozygotes are NOT affected**
 - One working gene copy is sufficient to prevent symptoms
 - Unaffected heterozygotes are called "**carriers**" because they can pass on disease alleles along without having the disease themselves
- In order to be affected with an autosomal recessive disorder, one must inherit **two non-working gene copies** (one from each parent)
- Children with an autosomal recessive disorder are usually born to carrier parents who do not have the disease

Autosomal Recessive Inheritance

- Here are the risks when both parents are **unaffected carriers**



X-Linked Recessive Inheritance

- Here we are talking about mutations in genes on the **X chromosome** – one of the sex chromosomes
- In X-Linked inheritance, males and females are affected differently because:
 - Females have two (2) X chromosomes
 - Males only have one (1) X chromosome



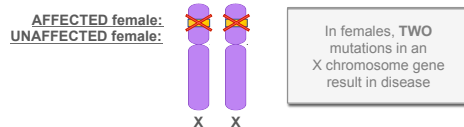
X-Linked Recessive Inheritance-Males

- An individual will be **unaffected** with an X-Linked disorder as long as he or she has **ONE WORKING** copy of the gene on the X chromosome
- Males** have a higher frequency of X-Linked disease because they only have one copy of the X chromosome and therefore only need **one mutation** to show disease, as there is no working copy of the gene on the Y chromosome



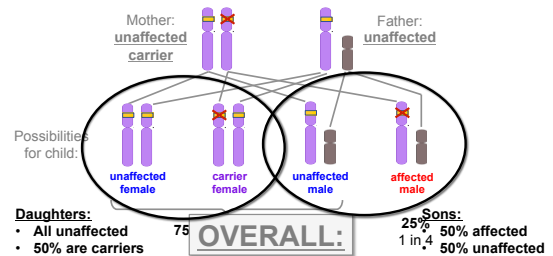
X-Linked Recessive Inheritance-Females

- An individual will be **unaffected** with an X-Linked disorder as long as he or she has **ONE WORKING** copy of the gene on the X chromosome
- Females** have a lower frequency of X-Linked disease because they have two copies of the X chromosome and require mutations in both to show disease (just as in autosomal recessive inheritance)
- Female heterozygotes** are **carriers** in X-Linked inheritance as well but can sometimes show symptoms of the disorder



X-Linked Recessive Inheritance

- Disease alleles are usually passed down through unaffected carrier females



Genetic Heterogeneity

- Genetic Heterogeneity** refers to genetic disorders caused by mutations in multiple different genes
- For example, a particular autosomal dominant disorder may be known to be caused by mutations in 5 separate genes
 - A mutation in any of these genes can cause the disorder
 - You do not need to have a mutation in all 5 genes, just a mutation in 1 of the 5 genes

Non-Mendelian Inheritance

- There are several non-Mendelian, forms of inheritance and we will mention two:
 - Multifactorial inheritance**
 - Mitochondrial inheritance**
- Less is known about these types of inheritance and they are very different from Mendelian inheritance

Multifactorial Inheritance

- Multifactorial diseases are named because they are influenced by **multiple factors**
- This usually means that changes in **many genes** (not just one) contribute to disease onset as well as **environmental factors**
 - We often do not know all of the genes involved
 - Environmental factors include anything that is not genetic
 - Examples include behaviors, nutrition, exposures, weight, etc.
- These diseases may cluster in families but we usually cannot see any clear inheritance patterns

Mitochondrial Inheritance

- Mitochondria are structures that produce energy and are found in the cytoplasm (not nucleus)
- Mitochondria have their own different, separate chromosome which carries different genes and DNA than the 46 chromosomes in the nucleus
- Mitochondrial DNA:
 - Is contained on **one, circular chromosome**
 - Codes for only 37 genes
 - Is **ALWAYS** and **ONLY** inherited from the **MOTHER**



Mitochondrial Inheritance



- In families with mitochondrial inheritance
 - All children (sons and daughters) of an affected female will be affected, but there is variability in the expression of the condition
 - Children of an affected male will **NOT** be affected

Other factors to consider

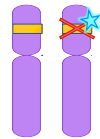
- In these last slides we will talk about a few things that can affect how inheritance looks in a family
 - Consanguinity
 - New mutations
 - Reduced penetrance

Consanguinity

- All humans are unaffected carriers of 8 to 10 **autosomal recessive** disorders
- Consanguineous families tend to show a higher rate of autosomal recessive disease, as parents who are related by blood are more likely to be carriers of the same disease

New Mutations

- New mutations can happen such that a change occurs spontaneously in a gene, causing an individual to be the first person affected in the family
- New mutations are also called *de novo* mutations and are most typically seen in **autosomal dominant** diseases, since one non-working gene can cause disease
- After the new mutation, the disease allele can be passed on in the same way as discussed earlier in this module as an autosomal dominant condition




Reduced Penetrance

- In some disorders, not all individuals with the disease genotype will display the disease phenotype
- **Reduced penetrance** means not every person with a disease mutation will have symptoms of the disease
- **Penetrance** is always expressed as a **percentage**:


$$\text{Penetrance} = \frac{\text{number of people with symptoms}}{\text{number of people who have disease mutation}}$$

Module 3 complete!

- Please take the Module 3 Knowledge Test




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MODULE 4:

MUTATIONS AND GENETIC TESTING

Module 4

Purpose:
To describe deleterious (harmful) effects on genes and chromosomes with respect to available testing options

Objectives:
Upon completing this module, participants should be able to:

1. Describe the general effect of chromosome abnormalities or mutations
2. Define available testing technologies and their limitations
3. Understand the benefits and risks of genetic testing

Causes of Genetic Disorders

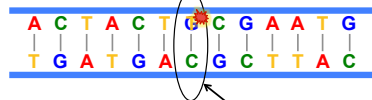
- Genetic disorders are caused by changes in genetic material (DNA or chromosomes) and are often suspected when multiple individuals in a family show the same symptoms
- The change in genetic material can occur in:
 - One single gene
 - More than one gene
 - An unknown gene or a gene that is not yet identified
- Genetic disorders can also be caused by a combination of genes and environmental factors

Mutations

- In Module 3, we defined **mutation** as a **change or alteration in the DNA sequence of a gene**
- A mutation may not have any effect but it can cause improper function of a protein, and ultimately, disease
- Here we will introduce three types of mutations:
 - Missense mutations**
 - Nonsense mutations**
 - Frameshift mutations**

Missense Mutations

- A **Missense Mutation** is a **single nucleotide change** which causes a single amino acid (building block of protein) to change
- Missense mutations are also called "point mutations"



now "C" is paired with "T" which is incorrect

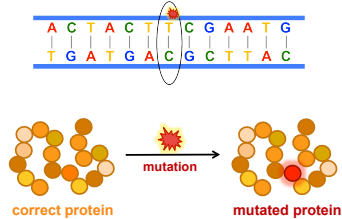
- In the example above, a guanine (G) was changed to a thymine (T) which changed one base pair in the DNA sequence

Remember that in DNA...

- "A" pairs with "T"
- "C" pairs with "G"

Missense Mutations

- During translation (the last step of the **Central Dogma**) a **Missense Mutation** will result in a single amino acid change.
- This creates a mutated protein.



Nonsense Mutations

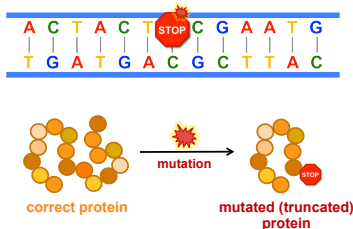
- A **Nonsense Mutation** is a single nucleotide change which causes single amino acid to STOP forming the protein
- The sequence change creates something called a **stop codon**
- Nonsense mutations result in truncated (shortened) proteins



- In the example above, a guanine (G) was changed to another nucleotide that will stop protein formation during translation at that location

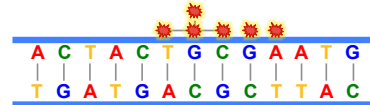
Nonsense Mutations

- The **Nonsense Mutation** will result an amino acid change that will stop translation (the last step of the **Central Dogma**).
- This creates a truncated (shortened) protein



Frameshift Mutations

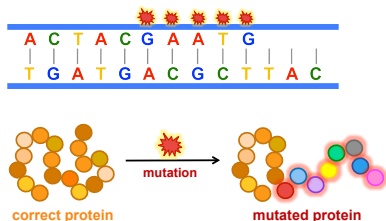
- A **Frameshift Mutation** occurs when multiple nucleotides in a DNA sequence are inserted or deleted.
- This causes a shift in the DNA sequence.
- Due to this shift, all amino acids after the insertion or deletion are changed.
- It may result in a stop codon



- Above is an example of a **DELETION** causing a frameshift mutation
- The entire sequence after the deletion is out of place, and thus incorrect
- If the mutation was an **insertion**, the effect would be the same but the sequence would shift in the **opposite direction**

Frameshift Mutations

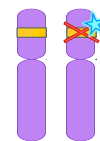
- The **Frameshift Mutation** will result in incorrect amino acids after the mutation during translation (the last step of the **Central Dogma**)
- This results in an abnormal protein product



New Mutations

- Recall from Module 3 that a **new mutation** can cause an individual to be the first person in the family to be affected by a genetic disorder

- New mutations are also known as **de novo mutations**



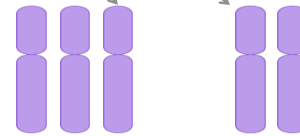
Chromosome Abnormalities

- We have now introduced the concept that types of **mutations in a single gene** can cause genetic disorders
- There are also other, **larger genetic changes** that can cause genetic disorders at a **chromosomal level**
 - Aneuploidy
 - Deletions and Duplications
 - Translocations

Chromosomal Abnormalities

Aneuploidy

- **Aneuploidy** is a genetic change that means an individual has an entire extra or missing chromosome in each cell



Chromosomal Abnormalities

Aneuploidy

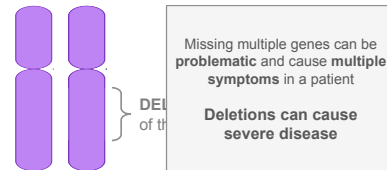
Some examples of Aneuploidy:

- **Trisomy** ("tri-" = three / "-somy" = chromosome) occurs when there are 3 copies of a chromosome instead of the expected 2 copies
 - The karyotype designation **47,XY,+21** tells us:
 - An extra chromosome is present (47 instead of 46)
 - This individual has 3 copies of chromosome 21 instead of 2 copies
 - This condition is Down syndrome, or Trisomy 21
- **Monosomy** ("mono-" = one / "-somy" = chromosome) occurs when there is 1 copy of a chromosome instead of the expected 2 copies
 - The karyotype designation **45,X** tells us:
 - A chromosome is missing (45 instead of 46)
 - This individual has only 1 copy of the X chromosome instead of 2 copies
 - This condition is Turner syndrome, or Monosomy X

Chromosomal Abnormalities

Chromosome Deletions

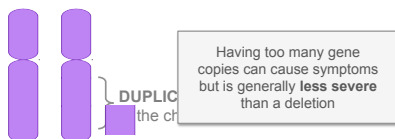
- **Chromosome deletions** occur when a piece of a chromosome is missing
 - It does not involve the entire chromosome
- Chromosome deletions may involve multiple genes



Chromosomal Abnormalities

Chromosome Duplication

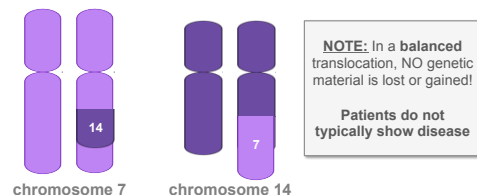
- **Chromosome duplications** occur when part of a chromosome is copied (duplicated) resulting in extra genetic material in the duplicated segment
 - It does not involve the entire chromosome
- Chromosome duplications cause over-expression or over-activity of multiple genes



Chromosomal Abnormalities

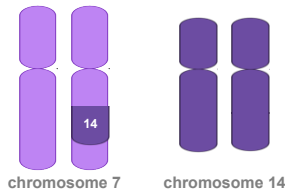
Translocations

- A **translocation** is an alteration in which a whole chromosome or broken segment of a chromosome becomes attached to or interchanged with another whole chromosome or segment
- A **balanced translocation** means that the segments **both reattach** to the other breakpoint



Translocations

- A **translocation** is an alteration in which a whole chromosome or broken segment of a chromosome becomes attached to or interchanged with another whole chromosome or segment
- A **unbalanced translocation** means that **only one** of the broken off pieces reattaches and the other is lost



NOTE: In an unbalanced translocation, genetic material is lost!

This example acts like a chromosomal deletion from chromosome 7

Introduction to Genetic Testing

Now we will discuss the genetic testing options that are used to detect the gene mutations and chromosomal abnormalities discussed in this module

Screening vs. Diagnostic Testing

- Genetic screening tests**
 - Used to identify individuals **at increased risk** for developing a genetic disease
 - Screening tests **DO NOT** give a diagnosis or confirm disease
- Diagnostic tests**
 - Diagnostic tests are specific to certain diseases and **DO NOT** address a patient's risk for **every** genetic disease or health problem
 - Diagnostic tests can confirm or deny the presence of a disease or condition
 - Give a "yes" or "no" answer

Why Genetic Testing?

- There are many scenarios that genetic testing could be beneficial for an individual or a family
- Some examples:*
- A couple who experiences multiple pregnancy losses/miscarriages
 - A child born with multiple birth defects
 - A family with a history of an illness or disease
 - A genetic test may provide a genetic diagnosis that can help prevent or manage symptoms and guide treatment

Benefits and Risks of Genetic Testing

- Benefits**
 - Gives patients more information
 - Can guide management and treatment
 - Can aid family planning decisions (i.e. recurrence risks)
- Risks**
 - Expensive cost
 - Emotional and social impact
 - Can be too much information for a patient to handle
 - Possibility of not finding an answer or diagnosis after multiple tests
- Genetic testing is a **PATIENT'S CHOICE** and they maintain the **right not to know**

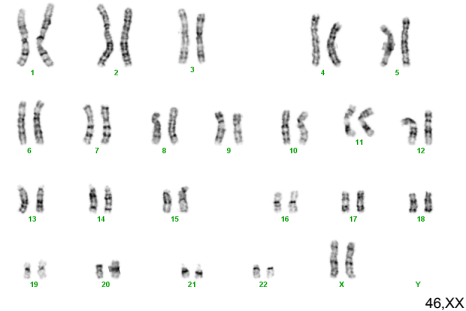
Genetic Testing Process

- Genetic testing is most often performed on a **blood sample**
- Generally, the 1st person in a family to have a genetic test should be **someone who is affected** with the disease or someone with the most severe symptoms
 - If a mutation or genetic abnormality is found, other family members can be tested for that specific change
 - If the same disease is "running in a family," it is usually caused by the same genetic change

Types of Testing - Karyotype

- We have already mentioned **Karyotype**, which evaluates the number and structure of every chromosome in a cell
 - A karyotype can also be called a "chromosome study"
- **Karyotyping can detect large scale genetic changes:**
 - Aneuploidy
 - Large chromosome deletions or duplications
 - Translocations
- **Karyotyping can NOT detect:** mutations in the DNA sequence

Types of Testing – Karyotype



Types of Testing – FISH

- **FISH** stands for **Fluorescent In Situ Hybridization**
- FISH is a test that looks for genetic changes on the chromosome level. However, FISH is typically performed for specific genetic conditions, rather than testing all of the chromosomes
- FISH probes tag specific sequences on a chromosome with a fluorescent label that acts like a magnet. Using a microscope, the testing laboratory counts the number of fluorescent signals in each cell
- 2 signals would indicate 2 copies of a specific sequence, 1 signal would indicate 1 copy of a specific sequence, and so on

Types of Testing – FISH

- **Can detect large scale genetic changes:**
 - Aneuploidy
 - Large chromosome deletions or duplications
 - Translocations

- **Can NOT detect:**
 - Mutations

Imagine 2 microscope fields to the left.

The green dots are fluorescent tags on a specific chromosome segment or region

Types of Testing – DNA Sequencing

- **DNA Sequencing** is a test that reads the nucleotide sequence of a specific gene
- It compares the individual's DNA sequence to the known genetic sequence to look for any changes
- **Can detect:** single base pair (missense, nonsense) mutations and small frameshift mutations
- **Can not detect:** deletions or duplications, chromosome abnormalities

Types of Testing – Del/Dup Analysis

- **Deletion/Duplication analysis** detects missing or extra pieces of DNA within a gene. In some cases it can detect if an entire gene is deleted or duplicated.
- For some genetic conditions, this test is performed as a secondary test if DNA sequencing is unable to detect a mutation
- Del/Dup analysis **DOES NOT** detect single base pair mutations or small frameshift mutations

Types of Testing – Genome Sequencing

- **Genome sequencing** is a new technology that has the ability to rapidly sequence all ~20,000 genes in an individual
- **Pros:** Looks at all known genes in one test
Can detect mutations
- **Cons:** Expensive cost
Returns massive amount of information
Will find many changes of unknown significance
May reveal genetic information a family or patient did not want to know (i.e. risk for another disease)

Genetic Test Results

- **Positive Genetic Test** = mutation or alteration found
 - For some disorders, a mutation is diagnostic
 - For other disorders, a mutation is not enough information to be diagnostic
 - Can also indicate a person is a **carrier** of a recessive disorder

Genetic Test Results

- **Negative Genetic Test** = no mutation or alteration found
 - Many tests cannot detect all mutations even in a single gene, so a negative result **does not** necessarily mean the person does not have a genetic disease
 - **Does not** mean a person's disease is not genetic or inherited
 - **Does not** mean that all possible genetic causes for a person's disease have been eliminated

A negative result means that a person does not have a mutation that is detectable by a particular genetic test

Module 4 complete!

- Please take the Module 4 Knowledge Test



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MODULE 5:

INHERITED CONGENITAL ANOMALIES
OF THE EYE

Module 5

Purpose:

To increase awareness of congenital ocular conditions that may have an inherited component and patients/families that may benefit from an overview of basic genetics education.

Objectives:

Upon completing this module, participants should be able to:

1. Describe the genetics of a subset of congenital ocular conditions
2. Identify patients/families with potentially inherited congenital ocular conditions

Characteristics of Disease

- We will begin by introducing some descriptors used when discussing diseases and conditions:
 - Congenital and Acquired
 - Isolated and Syndromic
 - Spectrum

“Congenital” and “Acquired”

- Used to describe the onset of a disease or malformation
 - **Congenital** means a disease or malformation was present **at birth**
 - Congenital conditions develop during embryonic or fetal stages
 - Congenital conditions are more likely due to an inherent **GENETIC** change, thus present at the time of conception
 - The genetic change is present in **every cell** of the body
 - **Acquired** means onset of a disease or malformation occurs **after conception or birth**
 - Acquired conditions may or may not be present at birth
 - Acquired conditions are more likely due to an **ENVIRONMENTAL** influence and may only affect parts of the body

“Isolated” and “Syndromic”

- Used to describe the symptoms of a **genetic** disease or malformation
 - **Isolated** means a genetic change resulted in a single symptom or manifestation
 - *Isolated coloboma* is caused by a genetic change, and coloboma is the only symptom that the patient displays
 - **Syndromic** means a genetic change results in a recurring pattern of symptoms, usually affecting different parts of the body
 - *Syndromic coloboma* is present in genetic disorders like CHARGE syndrome, where other symptoms such as hearing loss and heart defects are all caused by the same, single genetic change

Spectrum

- A **Spectrum** is a term used to describe a disease or condition that has a range of clinical symptoms and patients can be affected in differing degrees of severity (mild, moderate, severe)



Genetic Eye Disease

- It may seem difficult to know when to suspect an eye condition has a genetic cause
- There are certain characteristics that are more commonly seen when eye conditions are **GENETIC**:
 - Congenital / Early-onset
 - Bilateral
 - Multiple affected family members
 - Co-occurrence of other symptoms in other body parts

Genetic Eye Disease

- It is important to learn the **genetics** of eye disease because:
 - Approximately 33% of ALL genetic conditions have eye abnormalities
 - Cells in the eye express approximately 90% of the body's genes
 - About 50% of childhood blindness has a genetic cause

Genetic Overview of Eye Conditions

- We will now introduce known genetic causes and inheritance patterns of some inherited ophthalmic conditions you may see in the clinic
- Families with the following disorders may benefit from basic genetics education

Anophthalmia, Microphthalmia, and Coloboma

- **Anophthalmia** is the absence of the globe, but the external eye structures (lids, lashes, etc.) are intact
- **Microphthalmia** is a small eye, based on standardized measurements and the patient's age
- **Coloboma** is a closure defect in the eye, which may affect any of the tissues of the eye (commonly, the iris)
- These three malformations exist on a spectrum, where the mild end of the spectrum is coloboma and the severe end of the spectrum is anophthalmia. They also share common genetic causes.

Anophthalmia, Microphthalmia, and Coloboma

- They may be caused by a **chromosome abnormality** or by a **mutation** in multiple genes, most commonly:
 - *SOX2, RAX, PAX6, CHD7, SHH, SIX3, SIX6, and POMT1*
- The **inheritance** of these malformations is mostly **sporadic**, but can also be **autosomal dominant**, **autosomal recessive**, or **X-linked recessive**

Aniridia

- **Aniridia** is a malformation in which the iris is absent
- This condition can be caused by 2 separate genetic changes:
 - **Mutation in the *PAX6* gene:** This results in **isolated** aniridia
 - OR -
 - **Deletion that includes more than just the *PAX6* gene:**
 - This results in **syndromic** aniridia
 - When the deletion also involves the *WT1* gene, individuals are at increased risk to develop Wilms tumor as a young child
- **Autosomal dominant** inheritance or **sporadic** (especially with the deletion)

Glaucoma

- **Glaucoma** is a condition where an increased pressure within the eye results in damage to the optic nerve
- **Primary Congenital Glaucoma**
 - Caused by mutations in *CYP11B1* or *LTBP2*
 - **Autosomal recessive inheritance**
 - **Note:** The incidence of Primary Congenital Glaucoma is 1 in 3,300 in the Indian state of Andhra Pradesh, where the disease accounts for approximately 4.2% of all childhood blindness
- **Juvenile Open-Angle Glaucoma**
 - Caused mainly by mutations in *MYOC*, other less common genes exist
 - **Autosomal dominant inheritance** in most families but can be **autosomal recessive** in some families
 - "Juvenile" implies onset after 2 years of age
- **Infantile Glaucoma** can be a feature of many other syndromes

Congenital Cataracts

- A **Congenital Cataract** is a cloudiness in the lens of the eye, present at birth or within the first year of life
- It is known to be caused by certain **chromosome abnormalities** or by a **mutation** in multiple genes
- Many of the genetic causes have not yet been identified
- **Congenital Cataracts** can be seen following patterns of:
 - **Autosomal dominant** (most common)
 - Autosomal recessive
 - X-linked recessive

Retinitis Pigmentosa (RP)

- **Retinitis Pigmentosa** is a degeneration of the rod and cone cells in the retina, with onset as early as the first decade of life. It is characterized by night blindness, visual field constriction, and a particular pigmentation pattern on an eye exam
- There are **many genes** that can cause RP if mutated
- **RP** can be inherited in the following manners:
 - Autosomal dominant
 - Autosomal recessive
 - X-linked recessive
 - Mitochondrial

Leber's Congenital Amaurosis (LCA)

- **Leber's Congenital Amaurosis** is a disease involving severe retinal dystrophy in the first year of life which leads to significant vision loss
- The LCA phenotype can be caused by mutations in **many different genes**
- Inheritance is mainly **autosomal recessive**, although **autosomal dominant** has been reported in some families

Retinoblastoma (RB)

- A **Retinoblastoma** is a retinal tumor
- RB is caused by changes in the **RB1** gene including:
 - Mutations and deletions
 - Chromosome rearrangements involving chromosome 13q, where the gene is located
- **Autosomal dominant** inheritance or **sporadic**
- Genetic testing for this disorder includes chromosome analysis, and RB1 sequencing and deletion studies
 - Testing may be attempted on blood sample but may need to be done on tumor biopsy

CHARGE Syndrome

- **CHARGE syndrome** is an acronym where each letter stands for a symptom
 - C = **coloboma**
 - H = **heart defects**
 - A = **choanal atresia**
 - R = **retardation of growth/development**
 - G = **genital/urinary defects**
 - E = **ear anomalies**
- **CHD7** is the **only gene** that, when mutated, is known to cause CHARGE syndrome. Mutations in this gene account for about two-thirds (2/3) of cases.
- Most mutations are **sporadic**, and then inherited as **autosomal dominant** in future generations

Patients DO NOT need to have all 6 symptoms to have a diagnosis of CHARGE syndrome

Leber's Hereditary Optic Neuropathy (LHON)

- **Leber's Hereditary Optic Neuropathy** is a form of painless, bilateral vision loss. Usually loss of vision occurs in one eye, and vision loss in the other eye follows a few months later.
 - Males are 5 times more likely to be affected than females
- The majority of LHON cases are caused by **4 mutations** in the mitochondrial DNA (mtDNA, circular chromosome)
- **Mitochondrial inheritance (maternal)**

Ophthalmic Genetic Testing

- If ophthalmologists at your institute are interested in offering genetic testing, it will be necessary to investigate which tests are available in your area
- Tests to investigate include karyotype/chromosome analysis, gene sequencing, deletion/duplication study, FISH

Ophthalmic Genetic Testing

- **Possible test results:**
 - **Positive:** A known disease-causing mutation identified
 - **Negative:** No mutation identified
 - **Variant of Uncertain Significance:** A genetic change was identified but it has never been reported or proven to cause disease. No diagnostic conclusions can be drawn and further evaluation is necessary.
- The technology of genetic testing is imperfect. If no mutation is found (negative test), an individual may still have an inherited ophthalmic condition that cannot be found using available testing options

Module 5 complete!

- Please take the Module 5 Knowledge Test



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MODULE 6:

TALKING TO A PATIENT I –
PATIENT EDUCATION BASICS

Module 6

Purpose:

To describe basic methods for communicating fact-based health information to patients

Objectives:

Upon completing this module, participants should be able to:

1. Communicate basic genetic information to patients and families
2. Understand the purpose of providing patients with genetic information

Educating Patients in Genetics

- Giving patients genetic information is a complex task, and you should know **WHY** you are doing it
- The **main reason** for giving patients basic genetic education is so they **better understand their health**
- A genetic diagnosis may be able to **improve the TREATMENT AND MANAGEMENT** of a patient's eye problems

Educating Patients in Genetics

- The goal **IS NOT** to teach patients every detail about genetics and inheritance
- Rather, the goal **IS** to teach patients **basic information** that is relevant to their health
- You can expect **barriers** that will affect the way your patient understands what you say about genetics including their:
 - Educational background
 - Cultural practices
 - Language

The Role of Genetic Educator

- A Genetic Educator will meet briefly with patients who may benefit from genetic education, as determined by their ophthalmologist by review of their medical chart
- The patient will meet with a Genetic Educator **BEFORE** seeing the ophthalmologist
- The role of a Genetic Educator is to complete a family pedigree and define general terms prior to the patient receiving *personalized* genetic information from the ophthalmologist

The Role of a Genetic Educator

- Genetic information may be difficult for a lay person to understand
- Ways to help improve understanding may include:
 - The job of a Genetic Educator is to explain genetic concepts in a **simplified way** using easy-to-understand wording
 - **SPEAK CLEARLY!**
 - Stop to ask if they understand the information already discussed
- As a Genetic Educator, it is important to be **informative**, but at the same time **respectful** and **sensitive**

In a Patient Session...

- After introducing yourself as a Genetic Educator, the session will begin by **taking a family pedigree**
 - How to draw a family pedigree will be detailed in Module 7
- Taking a pedigree is an extremely important part of a genetics consultation because:
 - It provides useful information about the medical history of other family members
 - It is **organized so that it acts as a visual tool that may aid in diagnosis and identifying an inheritance pattern**
 - **Note of Caution:** It **DOES NOT** usually provide enough information to make a genetic diagnosis on its own and should be interpreted by the ophthalmologist

In a Patient Session...

- A family pedigree provides useful information for:
 - The Patient
 - The Patient's Family
 - The Ophthalmologist
- After you take the pedigree, it should be **kept in the patient's medical chart or file**

In a Patient Session...

- The session will include explanation of basic terms learned throughout this course including:
 - *Sporadic and Inherited*
 - *Congenital and Acquired*
 - *Isolated and Syndromic*
 - *Potential inheritance patterns*
(Mendelian and non-Mendelian, as relevant)

In a Patient Session...

- It is important to try to present the information in an unbiased manner
- It is important to stress that we have no control over the genes we inherit or the genes we pass on to our children
 - Some parents may feel a sense of guilt or blame and it is important to make it clear that this is something beyond our control
- Try not to present the concept of non-working gene copies as something that is wrong with the patient

In a Patient Session...

- Allow patients to ask questions **AT ANY TIME** during your conversation
- If you do not know the answer to a patient's question, it is important to be honest and direct the question to the ophthalmologist
 - **DO NOT** make up an answer to appear informed
- It is never appropriate to use the names of **other** patients in your conversation

Importance of Communication


- **The way in which you communicate is one of the most important aspects of being a good Genetic Educator**
- As we have mentioned, you must speak **slowly** and **clearly** so the information is conveyed to the patient in a way they can understand
- Genetics may be intimidating, scary, or confusing to a patient so it is extremely important to be respectful

Importance of Communication

- Being an effective communicator involves more than talking. It also requires that you:
 - Be an active **LISTENER**
 - Check in with the patient to ask about their understanding during the session
 - Speak clearly and clarify what you say so you are sure the patient understands
 - Be confident about the information that you present, while also being honest when you do not know the answer to a question

Module 6 complete!


- Please take the Module 6 Knowledge Test




Children's
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GENETIC EDUCATOR TRAINING COURSE



University of Pittsburgh Graduate School of Public Health



World Society of Paediatric Ophthalmology and Strabismus

MODULE 7:

TALKING TO A PATIENT II –
TAKING A FAMILY PEDIGREE

Module 7

Purpose:
To provide a foundation for obtaining family health histories and generating a pedigree.

Objectives:
Upon completing this module, participants should be able to:

1. Communicate with patients and families for the purpose of obtaining family health histories
2. Understand the basic relationships and symbols used in pedigrees
3. Draw a pedigree using standardized nomenclature

The Pedigree

- Module 6 introduced the pedigree as an important visual tool which provides family health information that is helpful for the patient, the patient's family, and the ophthalmologist
- Now we will introduce how to collect the information needed as well as how to draw a pedigree using correct symbols

A 3-Generation Pedigree

- A useful pedigree includes **THREE (3) GENERATIONS**
- If your patient is a child, include their generation, their parents' generation, and their grandparents
- If your patient is an adult:
 - If they have children, include their children's and their parent's generation
 - If no children, include their parents' generation and their grandparents

Comprehensive or Targeted

- A **COMPREHENSIVE** family history collects information about any and all health problems for each family member. This provides a very broad, complete picture of the family's health
- A **TARGETED** family history only asks for information regarding specific health problems.

Basic Pedigree Symbols

- On a pedigree, each family member is represented by a shape.

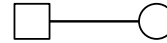
- MALES** are represented by a **SQUARE** 

- FEMALES** are represented by a **CIRCLE** 

- Family members of **unknown sex** are represented by a neutral **DIAMOND** 

Family Relationships

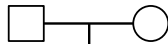
- On a pedigree, a **familial relationship** is represented by a **STRAIGHT LINE**



This **horizontal line** connecting a male and a female indicates a **MARRIAGE** or that the two individuals have **had children** together.

Family Relationships

- On a pedigree, a **familial relationship** is represented by a **STRAIGHT LINE**



A **vertical line** indicates **OFFSPRING**.

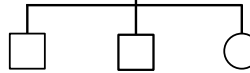
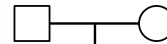
If this couple had **1 son**, it would be drawn like this:



Family Relationships

- On a pedigree, a **familial relationship** is represented by a **STRAIGHT LINE**

If this couple had **more than one child**, it would be drawn like this:

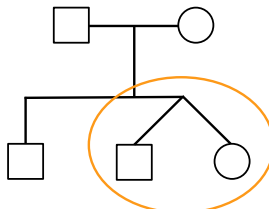


This family has 2 sons and 1 daughter. Brothers and sisters are depicted as coming down (descending) vertically from the same horizontal line.

Family Relationships

Twins

- Twins are shown as two diagonal lines beginning from the same point

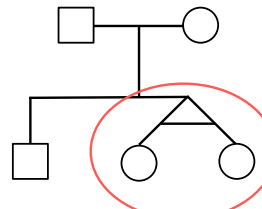


This depicts **FRATERNAL** twins (dizygotic)

Family Relationships

Twins

- Twins are shown as two diagonal lines beginning from the same point

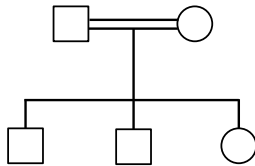


The addition of an extra horizontal line indicates **IDENTICAL** twins (monozygotic)

Family Relationships

Consanguinity

- **Consanguineous couples** (when a mother and father of a child are related by blood) are connected by a **DOUBLE HORIZONTAL LINE**



*Offspring of consanguineous couples are at increased risk for autosomal recessive disorders, as related parents are more likely to be carriers of the same disorders

Basic Pedigree Symbols

Deceased Individuals

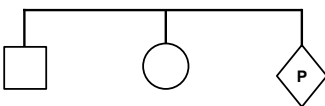
- Any individual who has passed away, has a diagonal line through the symbol:



Basic Pedigree Symbols

Pregnancy

- If a woman is pregnant, the pregnancy is represented by a diamond with a "P" written inside
- The pregnancy is placed in the same line as the future siblings, but note that it is **not yet** a CURRENT CHILD

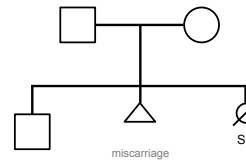


This shows 2 CURRENT children and 1 pregnancy

Basic Pedigree Symbols

Pregnancy Losses

- **Miscarriage:** Represented as a small, slightly raised triangle in the row of children/siblings
- **Stillbirth:** Represented as a small, slightly raised symbol (square for male, circle for female) with a diagonal line through it, with the letters "SB" underneath



This family shows a couple with 1 living son, 1 miscarriage, and 1 female stillbirth

NOTE: It is not necessary to write "miscarriage" below the triangle, but it IS standard to write "SB" below a stillbirth

The Proband

- The **PROBAND** is your **current patient** who is to be evaluated by the ophthalmologist
 - Your proband can be any age: If you work in pediatrics, the proband will be the child or minor
- The proband is indicated on a pedigree by drawing a **DIAGONAL ARROW** to his or her symbol, shown below

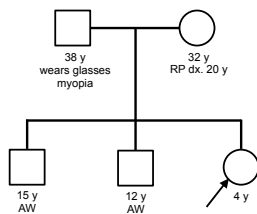


Collecting the Information

- As a Genetic Educator in Ophthalmology, it will be best to take a more targeted approach to taking a family pedigree (instead of comprehensive)
- For each family member, you should write down:
 - **AGE:** an individual's current age, or if the individual has died, the age at which he or she passed away
 - **ANY VISION PROBLEMS:** Describe briefly
 - Ex: Wears glasses, myopia
 - **ANY DIAGNOSES of EYE DISORDERS:** Include age at diagnosis
- All of this information is written directly below the corresponding individual's symbol

Collecting the Information

- Example below
 - *Note this is only a 2-generation pedigree



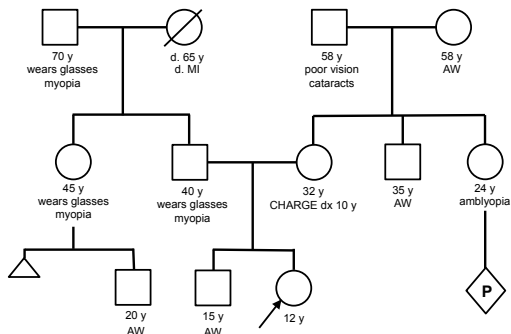
The mother, current age 32, was diagnosed (dx) at age 20 with Retinitis Pigmentosa (RP)

"AW" stands for "alive and well" indicating no known health concerns

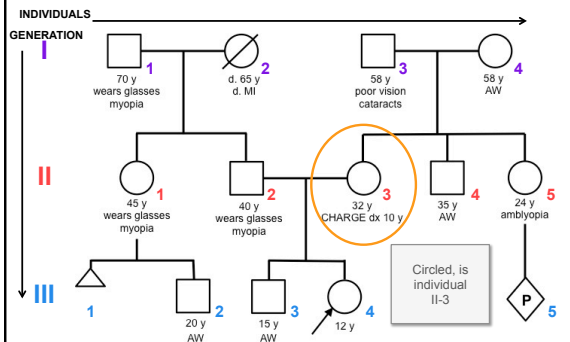
Collecting the Information

- The best way to learn to draw pedigrees is to practice and develop your own personal process
- We will demonstrate an example of an order to follow

In the narrated version, this will be a mock conversation with the patient, with details appearing as they reveal information



Referring to a Pedigree



Referring to a Pedigree

- You may also ask for the names of each family member, if it is helpful for you to keep track

• For example,

Holly
26 y
wears contacts
astigmatism
lazy eye in childhood

Special Notations

- Now we will discuss ways to label the symbols in a pedigree if there are known disease diagnoses

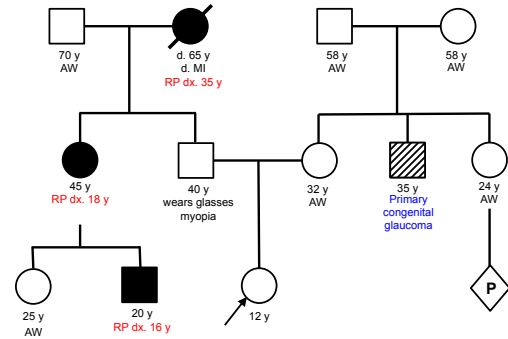
Family Disease Diagnoses

- If there is a known disease that has been diagnosed in a family individual, or in multiple family members, you can record this in an easy-to-see manner
- Instead of simply writing the disease name under the symbol, fill in the symbol to show the individual is AFFECTED with a known disease or disorder

unaffected male

AFFECTED male

Family Disease Diagnoses



Carriers

- **Carriers**, or unaffected heterozygotes, are possible in families seeing patterns of autosomal recessive or X-linked recessive inheritance
- Carriers are drawn on a pedigree as a symbol with a dot in the middle

Male carrier

Female carrier

- While unaffected, carriers have a 50% chance to pass on a non-working gene copy, and 50% chance to pass on a working gene copy

Module 7 complete!

- Please take the Module 7 Knowledge Test

APPENDIX E

KNOWLEDGE ASSESSMENT ANSWER KEYS

MODULE 1: MOLECULAR BIOLOGY – ANSWER KEY

1. DNA is composed of:

- a. Protein
- b. Cells
- c. Amino acids
- d. **Nucleotides**

Choice (a.) is incorrect. Protein is the product of the last step in the Central Dogma (DNA → RNA → Protein). DNA is not made of protein; rather, discrete DNA sequences, called genes, create proteins.

Choice (b.) is incorrect. Cells are the basic building blocks of the body which contain DNA within their nucleus.

Choice (c.) is incorrect. Amino acids are the basic building blocks of protein.

Choice (d.) is correct. Nucleotides are the basic building blocks of DNA.

2. The four DNA nucleotides are:

- a. Adenine, Cytosine, Guanine, Uracil (A, C, G, U)
- b. **Adenine, Cytosine, Guanine, Thymidine (A, C, G, T)**
- c. Adenine, Cytosine, Pyrimidine, Purine (A, C, P, P)
- d. Adenine, Guanine, Pyrimidine, Thymidine (A, G, P, T)

Choice (a.) is incorrect. Adenine (A), cytosine (C), and guanine (G) are DNA nucleotides. However, uracil (U) is a RNA nucleotide and is not present in DNA.

Choice (b.) is correct. The four nucleotides of DNA are adenine (A), cytosine (C), guanine (G), and thymidine (T).

Choice (c.) is incorrect. Adenine (A) and cytosine (C) are DNA nucleotides. However, pyrimidine and purine are classifications of nucleotides. To be specific, the DNA nucleotides cytosine (C) and thymidine (T) are pyrimidines and adenine (A) and guanine (G) are purines.

Choice (d.) is incorrect. Adenine (A), cytosine (C), and thymidine (T) are DNA nucleotides. However, pyrimidine is a classification of nucleotides. To be specific, the DNA nucleotides cytosine (C) and thymidine (T) are pyrimidines.

3. The structure of DNA is:

- a. Folded
- b. Single-stranded
- c. **Double-stranded**
- d. Triple-stranded

Choice (a.) is incorrect. DNA structures are not folded. This is a behavior of newly created proteins.

Choice (b.) is incorrect. DNA is a double-stranded molecule, whereas RNA is single-stranded.

Choice (c.) is correct. DNA is a double-stranded molecule that is twisted into a double helix.

Choice (d.) is incorrect. DNA is a double-stranded molecule and does not exist in a triple-stranded state.

4. DNA nucleotides (A, C, G, T) on the two strands bond to form base pairs. Which nucleotide ALWAYS pairs with C?
- A
 - C
 - G**
 - T

Choice (a.) is incorrect. The DNA nucleotide adenine (A) always pairs with thymidine (T).

Choice (b.) is incorrect. A cytosine (C) to cytosine (C) pairing is not possible because the DNA nucleotides are unable to pair with themselves. The DNA nucleotide cytosine (C) always pairs with guanine (G).

Choice (c.) is correct. The DNA nucleotide cytosine (C) always pairs with guanine (G).

Choice (d.) is incorrect. The DNA nucleotide thymidine (T) always pairs with adenine (A).

5. DNA nucleotides (A, C, G, T) on the two strands bond to form base pairs. Which nucleotide ALWAYS pairs with A?
- A
 - C
 - G
 - T**

Choice (a.) is incorrect. An adenine (A) to adenine (A) pairing is not possible because DNA nucleotides are unable to pair with themselves. The DNA nucleotide adenine (A) always pairs with thymidine (T).

Choice (b.) is incorrect. The DNA nucleotide cytosine (C) always pairs with guanine (G).

Choice (c.) is incorrect. The DNA nucleotide guanine (G) always pairs with cytosine (C).

Choice (d.) is correct. The DNA nucleotide adenine (A) always pairs with thymidine (T).

6. The three main types of RNA are mRNA, tRNA, and rRNA. What does the “m” in mRNA stand for?
- Mitosis
 - Meiosis
 - Messenger**
 - Molecular

Choice (a.) is incorrect. Mitosis is a process of cell division that generates new cells. Mitosis has no relationship to RNA.

Choice (b.) is incorrect. Meiosis is a process of cell division that generates reproductive cells. Meiosis has no relationship to RNA.

Choice (c.) is correct. Messenger (m) RNA is created in the nucleus from a DNA sequence. Then, it is transported into the cytoplasm where the mRNA is read by a ribosome, creating a specific protein. Messenger (m) RNA plays a primary role in the second step of the Central Dogma (DNA → RNA → Protein), acting as the “message” between DNA sequences and protein translation.

Choice (d.) is incorrect. The word “molecular” or “molecule” refers to small, fundamental units that contribute to the function of a larger structure.

7. The structure of mRNA is:

- a. Folded
- b. Single-stranded**
- c. Double-stranded
- d. Triple-stranded

Choice (a.) is incorrect. RNA structures are not folded. This is a behavior of newly created proteins.

Choice (b.) is correct. RNA is a single-stranded molecule.

Choice (c.) is incorrect. RNA is single-stranded molecule, whereas DNA is double-stranded.

Choice (d.) is incorrect. RNA is a single-stranded molecule and does not exist in a triple-stranded state.

8. The flow of information from DNA → RNA → protein is known as:

- a. The Genetic Code
- b. The Central Dogma**
- c. The Golden Rule
- d. The Tree of Life

Choice (a.) is incorrect. “The Genetic Code” is a term that is often used to describe DNA or RNA. However, it generally does not include protein.

Choice (b.) is correct. “The Central Dogma” is the term used to describe the process and flow of information from DNA to RNA to Protein.

Choice (c.) is incorrect. “The Golden Rule” is not a scientific term. Rather, it has many meanings, such as an infallible truth or expectation in a field of study or the principal of treating others the way you would like to be treated.

Choice (d.) is incorrect. “The Tree of Life” has many meanings. In the sciences, it is a branched diagram that illustrates the evolutionary relationship of all living creatures.

9. What does “transcription” do?

- a. Reads DNA to make mRNA**
- b. Makes DNA
- c. Divides cells
- d. Reads mRNA to make protein

Choice (a.) is correct. Transcription describes the first to second step of The Central Dogma, or using DNA sequences to generate mRNA.

Choice (b.) is incorrect. DNA is replicated from itself in a separate process from The Central Dogma.

Choice (c.) is incorrect. Cell division is not part of The Central Dogma and has no relationship to transcription.

Choice (d.) is incorrect. This response is describing the process of “translation.” Translation is the second to third step of The Central Dogma, where mRNA sequences and tRNA molecules are used to generate protein.



GENETIC EDUCATOR TRAINING COURSE

10. Where in the cell does “transcription” happen?

- a. Cytoplasm
- b. Nucleus**
- c. Mitochondria
- d. Lysosome

Choice (a.) is incorrect. The cytoplasm is a semi-fluid substance that fills a cell. The term cytoplasm is also used to describe the entire cell area that is not within the nucleus. With regard to The Central Dogma, translation (the step of RNA → Protein) occurs in the cytoplasm.

Choice (b.) is correct. The nucleus is the central hub of a cell and the location of DNA. As DNA is used to create RNA, transcription occurs in the nucleus.

Choice (c.) is incorrect. Mitochondria are the “powerhouses” of a cell. .

Choice (d.) is incorrect. Lysosomes are digestive structures inside a cell. Their main role is to process or destroy materials that the cell no longer requires. No step of The Central Dogma occurs in the lysosomes.

11. What does “translation” do?

- a. Reads DNA to make mRNA
- b. Makes DNA
- c. Divides cells
- d. Reads mRNA to make protein**

Choice (a.) is incorrect. DNA sequences are read to make mRNA through transcription. This is the first to second step of The Central Dogma.

Choice (b.) is incorrect. DNA is replicated from itself in a separate process from The Central Dogma.

Choice (c.) is incorrect. Cell division is not part of The Central Dogma and has no relationship to translation.

Choice (d.) is correct. Translation describes the second to third step of The Central Dogma, or using mRNA sequences and tRNA molecules to generate protein. This is distinct from choice (b.) because translation is the process of reading the mRNA sequence and signaling tRNAs (literally, “translating” the mRNA message into the final product - protein).

12. Where in the cell does “translation” happen?

- a. Cytoplasm**
- b. Nucleus
- c. Mitochondria
- d. Lysosome

Choice (a.) is correct. The cytoplasm is a semi-fluid substance that fills a cell. The term cytoplasm is also used to describe the entire cell area that is not within the nucleus. With regard to The Central Dogma, translation (the step of RNA → Protein) occurs in the cytoplasm.

Choice (b.) is incorrect. The nucleus is the central hub of a cell and the location of DNA. The mRNA is transported out of the nucleus and into the cytoplasm before translation can begin. No proteins are made within the nucleus.

Choice (c.) is incorrect. Mitochondria are the “powerhouses” of a cell, located in the cytoplasm and their role is to create energy for cell functions. .

Choice (d.) is incorrect. Lysosomes are digestive structures inside a cell, located in the cytoplasm. Their main role is to process or destroy materials that the cell no longer requires. No step of The Central Dogma occurs in the lysosomes.

13. What functional molecules perform most of the jobs of the cell?

- a. **Proteins**
- b. Membranes
- c. Ribosomes
- d. Endosomes

Choice (a.) is correct. Proteins are the final product of discrete DNA sequences called genes. Protein is a generalized term for the functional molecules in cells. As a group, proteins have a wide range of functions and participate in all cellular activities.

Choice (b.) is incorrect. Membranes are thin structures that act as dividers within and between cells. For example, the plasma membrane surrounds the entire cell and keeps all of its contents contained. There is also a plasma membrane around the nucleus, which keeps the nucleus and cytoplasm separated.

Choice (c.) is incorrect. Ribosomes are structures located in the cytoplasm of the cell. Ribosomes are the functional molecules in translation, as they help with the process of converting an mRNA sequence into its protein product.

Choice (d.) is incorrect. Endosomes are capsule-like structures that are created when the cell's exterior plasma membrane folds in onto itself. Endosomes take in materials from outside the cell, where these materials may be digested in lysosomes or be deposited back outside of the cell.

14. Proteins are made up of:

- a. Nucleotides
- b. Chromosomes
- c. Mitochondria
- d. **Amino acids**

Choice (a.) is incorrect. Nucleotides are the basic building blocks of DNA.

Choice (b.) is incorrect. Chromosomes are a condensed form of DNA that is visible under a microscope. Proteins participate in the organization of chromosomes ?is this going to confuse them?; however, the opposite is not true and chromosomes are not a component of proteins.

Choice (c.) is incorrect. Mitochondria are the "powerhouses" of the cell. Although numerous proteins have a function within the mitochondria, the mitochondria are not components of protein.

Choice (d.) is correct. Amino acids are the basic building blocks of proteins. There are 20 amino acids that are used to build protein. During translation, mRNA sequences signal tRNA molecules, to which amino acids are attached and a protein is made.

15. In order to work correctly, proteins must:

- a. Be translated from mRNA
- b. Be folded correctly
- c. Have the correct sequence of amino acids
- d. **All of the above**

Choice (a.) is incomplete. Proteins are translated from mRNA as a step in The Central Dogma. Although this is correct, there are other responses to this question that are also true.

Choice (b.) is incomplete. Protein function relies on proper folding and organization. If a protein is not folded properly, it may be missing key structures that allow it to perform its job in the cell. Although this is correct, there are other responses to this question that are also true.

Choice (c.) is incomplete. Proteins must have a correct sequence of amino acids, which follow the mRNA sequence. Although this is correct, there are other responses to this question that are also true.

Choice (d.) is correct. All of the above responses are true about proteins and their function.

MODULE 2: CELL CYCLE AND GENETICS

1. The study of inherited differences found in and between human populations and individuals is called:
- Biochemistry
 - Medicine
 - Genetics**
 - Evolution

Choice (a.) is incorrect. Biochemistry is the study of the chemical processes in living organisms.

Choice (b.) is incorrect. Medicine is the practice of diagnosing, treating, and preventing disease.

Choice (c.) is correct. **Genetics is the study of inheritance and inherited characteristics or differences in living organisms, such as humans.**

Choice (d.) is incorrect. Evolution is the change or progress of inherited characteristics over generations, contributing to the development of populations.

2. Humans have ____ pairs of chromosomes:
- 46
 - 26
 - 23**
 - 72

Choice (a.) is incorrect. Humans have 46 individual chromosomes, not 46 pairs of chromosomes.

Choice (b.) is incorrect. Humans have less than 26 pairs of chromosomes.

Choice (c.) is correct. **Humans have 23 pairs of chromosomes, totaling 46 individual chromosomes.**

Choice (d.) is incorrect. Humans have less than 72 pairs of chromosomes.

3. The 22 pairs of chromosomes that are NOT sex chromosomes are called:
- Autosomes**
 - Germline
 - Lysosomes
 - X and Y

Choice (a.) is correct. **Autosomes (chromosome pairs 1-22) are chromosomes that carry genes involved with physical characteristics, but not gender. Both males and females have 22 pairs of autosomes.**

Choice (b.) is incorrect. "Germline" describes the cells that divide to form gametes, or egg and sperm cells.

Choice (c.) is incorrect. Lysosomes are digestive structures inside a cell. Their main role is to process or destroy materials that the cell no longer requires. They are not related to chromosomes.

Choice (d.) is incorrect. X and Y are the sex chromosomes, which control gender. Females have two X chromosomes, whereas males have one X and one Y chromosome.

GENETIC EDUCATOR TRAINING COURSE

4. Children resemble both their mother and father because:
- a. They have half of each of their genes**
 - b. They have all of their genes
 - c. By chance
 - d. Children do not resemble both their mother and father

Choice (a.) is correct. Children inherit half of their genetic information from their father and half of their genetic information from their mother. A father passes on one copy of every chromosome (1-22 and either X or Y) and a mother passes on one copy of every chromosome (1-22 and X or X). These chromosomes pair up at conception.

Choice (b.) is incorrect. Children do not inherit all of their parents' genes. Otherwise, they would inherit 46 chromosomes from each parent, totaling to 92 chromosomes. This is not compatible with life.

Choice (c.) is incorrect. It is not "by chance" that parents and children both have the same color eyes, hair, or other physical features. Children resemble their parents because they inherit genes that control these traits from each parent.

Choice (d.) is incorrect. Children will have some resemblance to their mother and father, as well as other family members, due to inherited traits.

5. A normal, female karyotype is written as:
- a. 46,XY
 - b. 23,XY
 - c. 46,XX**
 - d. 23,XX

Choice (a.) is incorrect. The karyotype 46,XY represents a normal male.

Choice (b.) is incorrect. The karyotype 23,XY does not exist. There are not enough chromosomes.

Choice (c.) is correct. The karyotype 46,XX represents a normal female.

Choice (d.) is incorrect. The karyotype 23,XX does not exist. There are not enough chromosomes.

6. A human sperm has ____ chromosomes:
- a. 46
 - b. 26
 - c. 23**
 - d. 13

Choice (a.) is incorrect. Sperm do not carry 46 chromosomes. This is incompatible with survival.

Choice (b.) is incorrect. Sperm do not carry 26 chromosomes. This is incompatible with survival.

Choice (c.) is correct. Sperm carry 23 chromosomes. A human sperm is created through meiosis, or a type of cell division that creates germ cells. Meiosis halves the number of chromosomes (46 → 23). This results in sperm that carry the correct number of chromosomes to fertilize an egg and contribute to normal human development.

Choice (d.) is incorrect. Sperm do not carry 13 chromosomes. This is incompatible with survival.

7. Eggs and sperm are made by:

- a. **Meiosis**
- b. Mitosis
- c. Replication
- d. Transcription

Choice (a.) is correct. Meiosis is a type of cell division that halves the number of chromosomes (46 → 23). This results in egg and sperm cells that carry 23 chromosomes each. This is the correct number of chromosomes for fertilization and normal human development to occur.

Choice (b.) is incorrect. Mitosis is a type of cell division that most of the body's cells use to generate new cells, as it maintains the normal number of chromosomes (46 → 46). Egg and sperm must have 23 chromosomes to allow fertilization and normal development, therefore mitosis cannot be used.

Choice (c.) is incorrect. Replication is the process through which DNA is copied. Although this is a step of any cell division, it is not the process used to create egg and sperm.

Choice (d.) is incorrect. Transcription describes the first to second step of The Central Dogma, or using DNA sequences to generate mRNA.

8. Meiosis creates cells with:

- a. **Half of the original genetic material**
- b. The same amount of genetic material
- c. Double the amount of genetic material
- d. Any of the above

Choice (a.) is correct. Meiosis is a type of cell division that halves the amount of genetic material, or chromosomes (46 → 23), in egg and sperm cells.

Choice (b.) is incorrect. Meiosis does not maintain the same amount of genetic material during cell division. However, mitosis maintains the same amount of genetic material, or chromosomes (46 → 46). Most of the body's cells use mitosis to generate new cells.

Choice (c.) is incorrect. No cell division process results in cells with double the amount of genetic material.

Choice (d.) is incorrect. Meiosis is a defined process resulting in cells with half of the original genetic material. It does not maintain or increase the amount of genetic material.

9. Mitosis creates cells with:

- a. Half of the original genetic material
- b. **The same amount of genetic material**
- c. Double the amount of genetic material
- d. Any of the above

Choice (a.) is incorrect. Mitosis does not create cells with half of the original genetic material.

However, meiosis is a type of cell division that halves the number of genetic material, or chromosomes (46 → 23), in egg and sperm cells.

Choice (b.) is correct. Mitosis maintains the same amount of genetic material, or chromosomes (46 → 46). Most of the body's cells use mitosis to generate new cells.

Choice (c.) is incorrect. No cell division process results in cells with double the amount of genetic material.

Choice (d.) is incorrect. Mitosis is a defined process resulting in cells with half of the original genetic material. It does not maintain or decrease the amount of genetic material.



GENETIC EDUCATOR TRAINING COURSE

10. The cell cycle has four (4) active phases. Three (3) of the phases are called G1 Phase, G2 Phase, and M Phase. What is the missing phase called, and what happens during it?

- a. T Phase; DNA Transcription
- b. T Phase; RNA Translation
- c. S Phase; Mitosis
- d. **S Phase; DNA Synthesis and Replication**

Choice (a.) is incorrect. There is no T phase in the cell cycle, nor is transcription a part of the cell cycle. Recall, transcription describes the first to second step of The Central Dogma, or using DNA sequences to generate mRNA.

Choice (b.) is incorrect. There is no T phase in the cell cycle, nor is translation a part of the cell cycle. Recall, translation describes the second to third step of The Central Dogma, or using mRNA sequences and tRNA molecules to generate protein.

Choice (c.) is incorrect. S phase is the correct answer; however, mitosis is not the process that occurs during the S phase.

Choice (d.) is correct. S phase is the correct answer. During S phase, a cell's DNA is synthesized, replicated, and divided among the cells created during the cell cycle.

11. What is happening during the G1 and G2 Phases of the cell cycle?

- a. Gene regulation
- b. **Growth**
- c. Genetic recombination
- d. None of the above

Choice (a.) is incorrect. Gene regulation is not part of the cell cycle. This process is more important for active cells, so that the appropriate genes are turned on (expressed) or off (silenced).

Choice (b.) is correct. Both the G1 and G2 phases are times of cellular growth. During G1, the cell is preparing for DNA synthesis (S phase). During G2, the cell doubles its total mass, creating two new cells of equal size.

Choice (c.) is incorrect. Genetic recombination is not part of the cell cycle. However, it is an essential part of meiosis that creates new combinations of genes to be passed onto children.

Choice (d.) is incorrect. This is incorrect, as G1 and G2 involve cellular growth (answer b).

12. What letter of the alphabet is used to describe the short arm of a chromosome?

- a. c
- b. **p**
- c. q
- d. x

Choice (a.) is incorrect. The letter "c" is not used to describe any part of a chromosome.

Choice (b.) is correct. The letter "p" is used to describe the short arm of a chromosome. It represents the French word "petit," meaning small.

Choice (c.) is incorrect. The letter "q" is used to describe the long arm of a chromosome.

Choice (d.) is incorrect. A capital letter "X" identifies one of the sex chromosomes. However, a lowercase letter "x" is not used to describe any part of a chromosome.



GENETIC EDUCATOR TRAINING COURSE

13. The correct order for organization of genetic material (from smallest to largest) is:

- a. Chromosome → Gene → Nucleotide
- b. Amino Acid → Protein → Enzyme
- c. Gene → Chromosome → DNA
- d. **Nucleotide → Gene → Chromosome**

Choice (a.) is incorrect. This is the reverse order, presented from largest to smallest.

Choice (b.) is incorrect. Amino acids, proteins, and enzymes are not involved in the organization of genetic material. Amino acids are basic building blocks of proteins and enzymes are proteins involved in biochemical reactions.

Choice (c.) is incorrect. DNA is smaller than a gene and a chromosome. Therefore, this order is not correct.

Choice (d.) is correct. Nucleotide → Gene → Chromosome is the correct order. Nucleotides are the basic building blocks of DNA, DNA sequences create distinct genetic instructions called genes, and many genes are lined up along the length of a chromosome.

14. Approximately how many genes are coded for in the human genome?

- a. 1,000
- b. **20,000**
- c. 50,000
- d. 2,000,000

Choice (a.) is incorrect. There are more than 1,000 genes in the human genome.

Choice (b.) is correct. There are approximately 20,000 genes in the human genome.

Choice (c.) is incorrect. There are less than 50,000 genes in the human genome.

Choice (d.) is incorrect. There are less than 2,000,000 genes in the human genome.

15. A piece of a gene that provides the code for a protein is called:

- a. **an Exon**
- b. an Instruction
- c. an Intron
- d. a Splice site

Choice (a.) is correct. An exon is the coding region of a gene that is transcribed from DNA → RNA during the first to second step of The Central Dogma.

Choice (b.) is incorrect. Generally, a gene may be referred to as an "instruction." However, this does not describe the specific piece of a gene that codes for a protein.

Choice (c.) is incorrect. An intron is a noncoding part of a gene that is transcribed from DNA → RNA during the first to second step of The Central Dogma. However, the process of splicing (occurring between transcription and translation) removes introns from mRNA before protein is generated.

Choice (d.) is incorrect. A splice site is a specific DNA sequence between exons (coding regions of a gene) and introns (non-coding regions of a gene). Splice sites act as a signal, indicating what parts of a gene can be removed before protein is generated.

MODULE 3: INHERITANCE

1. Inherited traits:
 - a. Are always present in every member of a family
 - b. Skip generations
 - c. **Are passed from parent to child**
 - d. None of the above

Choice (a.) is incorrect. At most, a child inherits half of a parent's genetic information or traits. Therefore, an inherited trait may only be present in some family members.

Choice (b.) is incorrect. Genes and inherited traits are passed directly from parent to child. Although some traits or diseases do not appear in successive generations, this is due to a particular inheritance pattern or multifactorial effects.

Choice (c.) is correct. **Inherited traits, controlled by genes, are passed from parent to child.**

Choice (d.) is incorrect. One of the above statements is true (see choice c).

2. Different forms of the same gene are called:
 - a. Loci
 - b. Nucleotides
 - c. **Alleles**
 - d. Homozygotes

Choice (a.) is incorrect. "Loci" (singular: locus) describes a position or place. This term is often used in genetics to describe the chromosomal location of a specific gene.

Choice (b.) is incorrect. Nucleotides are the basic building blocks of DNA, which encode genes.

Choice (c.) is correct. **"Allele" is the term used in genetics to describe different forms of the same gene. For example, there are three alleles for the gene that determines our blood type (allele A, allele B, or allele O).**

Choice (d.) is incorrect. A homozygote is a person who has the same allele at a particular locus.

3. A "disease-causing" allele can sometimes be called a "non-working copy" because there is a:
 - a. Mutation
 - b. Deletion
 - c. Duplication
 - d. **All of the above**

Choice (a.) is incorrect. A mutation can disrupt a gene and be disease-causing; however, this answer is incomplete.

Choice (b.) is incorrect. A deletion can disrupt a gene or genes and be disease-causing; however, this answer is incomplete.

Choice (c.) is incorrect. A duplication can disrupt a gene or genes and be disease-causing; however, this answer is incomplete.

Choice (d.) is correct. **Mutations, deletions, and duplications are all mechanisms by which a gene or genes can be disrupted and be disease-causing.**

4. A family pedigree in which every child has an affected parent is consistent with which pattern of inheritance?
- Autosomal Dominant**
 - Autosomal Recessive
 - X-Linked
 - Multifactorial

Choice (a.) is correct. One major characteristic of an autosomal dominant pedigree is that each child affected by the disorder also has an affected parent. This is because a parent, who has one non-working gene has a 50% chance to pass it on to each child, who will also be affected.

Choice (b.) is incorrect. Autosomal recessive pedigrees are characterized by multiple affected individuals in a single generation (brothers and sisters) or a single affected individual in a pedigree. Typically, parents of an affected child are unaffected carriers, not affected themselves.

Choice (c.) is incorrect. Affected and unaffected status in a X-linked pedigree depends on an individual's gender, where males are affected and females express few or no traits of the condition. Also, there is no male-to-male transmission of the condition. Therefore, not every affected child has an affected parent.

Choice (d.) is incorrect. Typically, a multifactorial condition affects a single individual in a family. Although the genetic factors or predisposition for the condition may be passed on, children would also need to be exposed to the environmental influences that contribute to the condition. Therefore, pedigrees displaying multifactorial conditions do not show a consistent pattern.

5. In autosomal dominant inheritance, an affected parent has a _____ chance to pass the affected gene to his or her child.
- 25%
 - 50%**
 - 75%
 - 100%

Choice (a.) is incorrect. There is greater than a 25% chance for an affected parent to pass the non-working gene for an autosomal dominant condition to his or her child.

Choice (b.) is correct. In autosomal dominant inheritance, an affected parent has a 50% (1 in 2) chance to pass on the non-working gene to his or her child, who will be affected. This also means that the affected parent has a 50% chance to pass on the working gene to his or her child, who will not be affected.

Choice (c.) is incorrect. There is no inheritance pattern associated with a 75% chance to pass on an affected gene.

Choice (d.) is incorrect. There is less than 100% chance for an affected parent to pass the non-working gene for an autosomal dominant condition to his or her child.

6. In classic autosomal recessive inheritance, a heterozygous individual with one working and one non-working gene copy will be:
- An unaffected carrier**
 - Affected with the disorder
 - Late onset
 - Any of the above

Choice (a.) is correct. An unaffected carrier (heterozygote) has one working gene and one non-working gene for an autosomal recessive disorder. They will have no related symptoms.

Choice (b.) is incorrect. To be affected with an autosomal recessive disorder, an individual must have two non-working genes (homozygous).

Choice (c.) is incorrect. Individuals with one working gene and one non-working gene (heterozygotes) for an autosomal recessive condition are not expected to develop the full disease at any age.

Choice (d.) is incorrect. An individual with one working gene and one non-working gene (heterozygote) for an autosomal recessive condition are unaffected carriers (see choice a).

7. In classic autosomal dominant inheritance, a heterozygous individual with one working and one non-working gene copy will be:
- An unaffected carrier
 - Affected with the disorder**
 - Late onset
 - Any of the above

Choice (a.) is incorrect. An unaffected carrier describes an individual with one working gene and one non-working gene (heterozygote) for an autosomal recessive disorder. This does not apply to autosomal dominant disorders because one non-working gene is sufficient to cause symptoms.

Choice (b.) is correct. An individual with one working gene and one non-working gene (heterozygote) for an autosomal dominant disorder will be affected. This is because one non-working gene is sufficient to cause symptoms.

Choice (c.) is incorrect. An individual with one working gene and one non-working gene (heterozygote) will be affected. The age of onset varies between conditions and can range from before birth to adulthood.

Choice (d.) is incorrect. An individual with one working gene and one non-working gene (heterozygote) for an autosomal dominant disorder will be affected (see choice b).

8. If two parents are both carriers (unaffected heterozygotes) of an autosomal recessive disorder, the chance they will have an affected child is:
- 0%
 - 25%**
 - 50%
 - 100%

Choice (a.) is incorrect. There is greater than a 0% chance that two parents who are carriers of an autosomal recessive disorder will have an affected child.

Choice (b.) is correct. When two parents are carriers for the same autosomal recessive condition, the following scenarios are possible: 25% (1 in 4) chance that both parents pass on their non-working gene and have an affected child; 50% (2 in 4) chance that one parent will pass on the working gene and one parent will pass on the non-working gene, and the child will be an unaffected carrier; 25% (1 in 4) chance that both parents pass on their working gene and the child will neither be affected nor a carrier.

Choice (c.) is incorrect. When two parents are carriers for the same autosomal recessive condition, there is a 50% (2 in 4) chance that the child will be an unaffected carrier. However, the risk for a child to be affected is less than 50%.

Choice (d.) is incorrect. There is less than a 100% chance that two parents who are carriers of an autosomal recessive disorder will have an affected child.

9. All individuals affected with an autosomal recessive disorder MUST have:
- One working and one non-working copy of a gene
 - Two non-working copies of a gene**
 - One affected parent
 - Two affected parents

Choice (a.) is incorrect. In autosomal recessive disorders, one working gene will prevent symptoms of the disorder.

Choice (b.) is correct. In autosomal recessive disorders, two non-working genes are not producing enough normal protein to perform its necessary function.

Choice (c.) is incorrect. This is not a requirement for autosomal recessive inheritance. Although an individual with an autosomal recessive disorder can have an affected parent, their unaffected parent must also be a carrier for the same condition and pass on their non-working gene for the child to be affected.

Choice (d.) is incorrect. This is not a requirement for autosomal recessive inheritance. Although an individual with an autosomal recessive disorder can have two affected parents, it is more common for two parents to be unaffected carriers.

10. In X-linked inheritance, males are affected differently than females because:

- a. Their hormones are different
- b. They produce sperm
- c. They have a different number of total chromosomes
- d. **They only have one (1) copy of the X chromosome**

Choice (a.) is incorrect. Hormone differences between males and females have no effect on the inheritance or expression of an X-linked disorder.

Choice (b.) is incorrect. The male reproductive system has no effect on an X-linked disorder.

Choice (c.) is incorrect. Males and females have the same number of chromosomes (46).

Choice (d.) is correct. Males and females differ by the sex chromosomes, where males have one X chromosome and one Y chromosome and females have two X chromosomes. When a male has a non-working gene on his X chromosome, there is no gene on his Y chromosome to mask the disorder; however, a female with a non-working gene on her X chromosome has a paired, working gene on her opposite X chromosome, which is sufficient to prevent symptoms.

11. If only 70% of individuals with a known disease genotype are affected by the disease phenotype, this disease most likely displays:

- a. **Reduced penetrance**
- b. A new mutation
- c. Multifactorial inheritance
- d. Autosomal recessive inheritance

Choice (a.) is correct. Reduced penetrance means that the percentage of individuals who carry a known genetic mutation and display symptoms divided by all who carry the known genetic mutation (those with symptoms and those without symptoms) is less than 100%.

Choice (b.) is incorrect. A new (*de novo*) mutation may occur in a person with an autosomal dominant or X-linked condition, particularly when they are the first person affected in their family.

Choice (c.) is incorrect. Multifactorial inheritance is the combination of genetic and environmental factors that contribute to the development or expression of a condition or trait.

Choice (d.) is incorrect. Autosomal recessive inheritance is characterized by a 25% chance to be affected when two parents are unaffected carriers. A person with an autosomal recessive disorder expresses symptoms, ranging from mild to severe. It is uncommon for a person to have the genetic mutations for an autosomal recessive disorder and have no signs or symptoms.

12. When multiple genes contribute to a disease phenotype, this is called:

- a. **Genetic heterogeneity**
- b. Reduced penetrance
- c. An Environmental factor
- d. X-linked inheritance

Choice (a.) is correct. Genetic heterogeneity (“hetero-” meaning different) describes a particular condition with numerous underlying genetic causes.

Choice (b.) is incorrect. Reduced penetrance describes the percentage of individuals with a known genetic mutation for a particular disease and who also display symptoms. This relationship is independent of how many genes are associated with a specific disorder.

Choice (c.) is incorrect. Environmental factors may influence the expression of a multifactorial condition. However, this is separate from the number of underlying genetic causes for a disorder.

Choice (d.) is incorrect. The inheritance pattern of a condition has no effect on the number of underlying genetic causes.

13. When many genes AND many environmental factors contribute to a disease phenotype, this is called:
- Autosomal dominant inheritance
 - Single-gene inheritance
 - Multifactorial**
 - Mitochondrial inheritance

Choice (a.) is incorrect. Autosomal dominant inheritance results when an individual has one non-working copy of a gene. Environmental factors do not influence how these conditions are inherited.

Choice (b.) is incorrect. Single-gene inheritance describes a genetic condition that is associated with only one underlying genetic cause without other influences, like multiple genes or the environment.

Choice (c.) is correct. Multifactorial inheritance is the combination of genetic and environmental factors that contribute to the development or expression of a condition or trait.

Choice (d.) is incorrect. Mitochondrial inheritance results from inheriting mutations in the mitochondrial DNA (mtDNA) from a mother. Although some mitochondrial conditions can be influenced by environmental factors, this is not a requirement for expression of a mitochondrial disorder.

14. Mitochondrial DNA:
- Has the same structure and shape as nuclear DNA
 - Is inherited from your father
 - Codes for more genes than nuclear DNA
 - Is inherited from your mother**

Choice (a.) is incorrect. Nuclear and mitochondrial DNA have different structures. Nuclear DNA exists as a double-stranded helix, which condenses into chromosomes prior to cell division, where mitochondrial DNA exists as a double-stranded, circular molecule.

Choice (b.) is incorrect. Mitochondrial DNA is not inherited from your father, as there are very few mitochondria in the head of the sperm that fertilizes an egg.

Choice (c.) is incorrect. There are approximately 20,000 genes in the nuclear DNA, compared to 37 genes in mitochondrial DNA.

Choice (d.) is correct. Mitochondrial DNA is inherited only from a mother. The egg cell contributes all of the mitochondria in a future child. The sperm only contributes the father's genetic information (DNA) when it fertilizes the egg.

15. If an individual is the first in their family affected with a disease (i.e. they did not inherit it from a parent), this may be due to:
- A new mutation**
 - Dominant inheritance
 - Mitochondrial inheritance
 - All of the above

Choice (a.) is correct. A new (*de novo*) mutation may occur in an individual with an autosomal dominant or X-linked condition, particularly when they are the first person affected in their family.

Choice (b.) is incorrect. An autosomal dominant inheritance pattern cannot account for a single affected family member. A characteristic of autosomal dominant inheritance is that every affected child has an affected parent.

Choice (c.) is incorrect. Mitochondrial inheritance may present with a single individual in a family; however, it is more common for multiple relatives through the maternal line to be affected.

Choice (d.) is incorrect. One of the above statements is true (see answer a).

MODULE 4: MUTATIONS AND GENETIC TESTING

1. A genetic disorder may be caused by:
 - a. One gene
 - b. More than one gene
 - c. An unidentified gene
 - d. All of the above**

Choice (a.) is incomplete. A genetic disorder may also be caused by more than just a single gene as well as an unidentified gene.

Choice (b.) is incomplete. A genetic disorder may also be caused by a single or unidentified gene as well as more than one gene.

Choice (c.) is incomplete. A genetic disorder may also be caused by a single known gene or more than one gene.

Choice (d.) is correct. A genetic disorder may be caused by all of the above, a single known gene, more than one gene and a yet unidentified gene.

2. Which of the following is a type of chromosome abnormality?
 - a. Deletion
 - b. Duplication
 - c. Aneuploidy
 - d. All of the above**

Choice (a.) is incomplete. A deletion is a form of chromosome abnormality resulting in missing chromosome material but duplications and aneuploidy are chromosome abnormalities as well.

Choice (b.) is incomplete. A duplication is a form of chromosome abnormality resulting in extra chromosome material but deletions and aneuploidy are also chromosome abnormalities.

Choice (c.) is incomplete. Aneuploidy (monosomy or trisomy) is a form of chromosome abnormality where there is an entire extra or missing chromosome but deletions and duplications are chromosome abnormalities as well.

Choice (d.) is correct. Deletions, duplications and aneuploidy are all examples of types of chromosome abnormalities.

3. In general, what type of chromosome abnormality has the most severe effect?
 - a. Deletion**
 - b. Duplication
 - c. Balanced translocation
 - d. They are equally severe

Choice (a.) is correct. A deletion of chromosome material typically presents with more severe symptoms since the individual is missing one copy of every gene carried in that region of the chromosome.

Choice (b.) is incorrect. Often duplications cause overexpression of a gene because there are 3 copies instead of two. This is generally less severe than a deletion of the same gene, but duplications of large regions may lead to severe disease.

Choice (c.) is incorrect. A balanced translocation typically does not result in loss or gain of chromosome material. Individuals with balanced translocations typically do not show disease.

Choice (d.) is incorrect. Individuals with deletions are typically more severely affected than those with duplications. Individuals with balanced translocations are typically unaffected. Therefore, they are not equally severe.

4. A mutation is defined as:
- a. A change or alteration in a gene**
 - b. Missing a chromosome
 - c. Having an extra chromosome
 - d. All of the above

Choice (a.) is correct. A mutation is defined as a change or alteration in a gene.

Choice (b.) is incorrect. Monosomy is when there is a missing chromosome. This is a type of aneuploidy, not a gene mutation.

Choice (c.) is incorrect. Trisomy is when there is an extra chromosome present in the cells. This is a type of aneuploidy, not a gene mutation.

Choice (d.) is incorrect. Only answer (a.) is correct.

5. Having a mutation may:
- a. Have no effect
 - b. Cause a protein to function improperly
 - c. Cause a disease
 - d. All of the above**

Choice (a.) is incomplete. Having a mutation may have no effect on the individual but it may also cause a disease.

Choice (b.) is incomplete. Having a mutation may cause a protein to function improperly but may not result in disease.

Choice (c.) is incomplete. Having a mutation may cause disease but it may also have no effect on the individual.

Choice (d.) is correct. Having a mutation may have no effect or it may also cause a disease due to improper functioning of the protein it codes.

6. What type of genetic mutation creates a stop codon?
- a. Missense mutation
 - b. Nonsense mutation**
 - c. Dominant mutation
 - d. Silent mutation

Choice (a.) is incorrect. A missense mutation will result in a single amino acid change, not a stop codon.

Choice (b.) is correct. A nonsense mutation is a sequence change which results in a stop codon which stops translation and truncates or shortens the protein.

Choice (c.) is incorrect. A dominant mutation describes the type of inheritance, meaning that it requires only one of the two genes to have a mutation in order to show symptoms of the disease. A dominant mutation may be a missense, nonsense or frame shift.

Choice (d.) is incorrect. A silent mutation is a DNA change which codes for the same amino acid or a similar one. A silent mutation does not change the functioning of the protein.

7. Another word for a “new” mutation is:

- a. **De novo**
- b. Unique
- c. Original
- d. Single

Choice (a.) is correct. A de novo mutation is one that is new in that individual and not found in either parent.

Choice (b.) is incorrect. A new mutation is not called unique.

Choice (c.) is incorrect. A new mutation is not called original.

Choice (d.) is incorrect. A new mutation is not called single.

8. What is genetic screening?

- a. Diagnosing individuals with genetic diseases or syndromes
- b. **Identifying individuals at increased risk for developing a genetic disease**
- c. Obtaining a family history of genetic disease
- d. Discussing genetics and testing with a patient

Choice (a.) is incorrect. A genetic screening test does not diagnose individuals with a genetic disease. This is called a diagnostic test.

Choice (b.) is correct. A genetic screening test is one which identifies individuals at increased risk for developing a genetic disease.

Choice (c.) is incorrect. Obtaining a family history of genetic disease is part of the genetic education session, not genetic screening.

Choice (d.) is incorrect. Discussing genetics and testing with a patient is part of the genetic education session, not genetic screening.

9. A benefit of genetic testing is:

- a. Gives patients more information
- b. Can improve management and treatment
- c. Can affect family planning decisions
- d. **All of the above**

Choice (a.) is incomplete. Genetic testing does give patients more information but it can also improve management and affect family planning.

Choice (b.) is incomplete. Genetic testing may improve the management and treatment of a patient if it confirms a diagnosis but it also provides more information to the patient and can affect family planning.

Choice (c.) is incomplete. Genetic testing may affect family planning decisions but it may also provide patients with more information and may improve management and treatment.

Choice (d.) is correct. All of the above listed statements are true of genetic testing.

10. What type of sample is most often used for genetic testing?

- a. **Blood**
- b. Hair root
- c. Skin
- d. The part of the body where the person has health problems

Choice (a.) is correct. Blood is the most often type of sample used for genetic testing.

Choice (b.) is incorrect. While hair root may be a source of DNA, it is not the most often used sample for testing.

Choice (c.) is incorrect. Skin may be used as a source of DNA but it requires a biopsy and is not the most often used sample for testing.

Choice (d.) is incorrect. Disease-causing genetic changes are generally found in every cell of the body, so it is not usually necessary to use tissue from the affected body part.

11. Generally, who in a family should be the first person to have a genetic test?

- a. **A person affected with the disorder**
- b. The father
- c. The mother
- d. The oldest person in the family

Choice (a.) is correct. The first person in a family who should be tested is a person affected with the disorder. This allows for the most accurate interpretation of the results and if positive, then allows for testing of other family members.

Choice (b.) is incorrect. The first person tested in a family should be an affected person, not a relative.

Choice (c.) is incorrect. The first person tested in a family should be an affected person, not a relative.

Choice (d.) is incorrect. The first person tested in a family should be an affected person, not a relative.

12. What is a reason to order genetic testing for a patient?

- a. The patient has experienced multiple pregnancy losses
- b. The patient has multiple congenital anomalies
- c. There is a family history of a particular disorder
- d. **All of the above**

Choice (a.) is incomplete. While a physician may order genetic testing for a couple experiencing multiple pregnancy losses, this is not the only correct answer.

Choice (b.) is incomplete. While a physician may order a genetic test for a patient with multiple congenital anomalies, this is not the only correct answer.

Choice (c.) is incomplete. While a physician may order a genetic test for an affected patient with a family history of a particular disorder, this is not the only correct answer.

Choice (d.) is correct. All of the answers listed above are potential reasons why a physician may order a genetic test for a patient.

13. What genetic test evaluates the structure and number of all chromosomes?

- a. DNA sequencing
- b. Genome sequencing
- c. FISH
- d. **Karyotype**

Choice (a.) is incorrect. DNA sequencing is a test which reads the nucleotide sequence. By comparing to the known coding sequence, it may detect single base pair mutations and small frame shift mutations within a single gene. It provides no information about the chromosomes.

Choice (b.) is correct. Genome sequencing is new technology which sequences thousands of genes but does not provide any information about the structure and number of chromosomes.

Choice (c.) is incorrect. FISH (Fluorescent *in situ* hybridization) is a special test used to detect changes of genetic material at the chromosome level. While it can provide information about a specific chromosome sequence, it does not evaluate the structure and number of all the chromosomes as an initial test.

Choice (d.) is correct. A karyotype is a test which evaluates the structure and number of all the chromosomes within a cell.

14. What genetic test can detect a single base pair mutation in a gene?

- a. **DNA sequencing**
- b. Deletion/Duplication analysis
- c. FISH
- d. Karyotype

Choice (a.) is correct. DNA sequencing is a test which reads the nucleotide sequence. By comparing to the known coding sequence, it may detect single base pair mutations and small frameshift mutations within a single gene.

Choice (b.) is incorrect. Deletion/Duplication studies are performed to determine if there are large pieces of extra or missing DNA sequence within a gene. This testing will not detect a single base pair mutation.

Choice (c.) is incorrect. FISH (Fluorescent *in situ* hybridization) is a special test used to detect changes of genetic material at the chromosome level. While it can provide information about a specific chromosome sequence, it does not detect single gene mutations.

Choice (d.) is incorrect. A karyotype is a test which evaluates the structure and number of all the chromosomes within a cell. It does not detect mutations in the DNA sequence.

15. What does a negative genetic test result mean?

- a. **A person does not have any of the mutations tested for in a certain gene**
- b. A person does not have any genetic diseases
- c. A person does not have a genetic cause for their disease
- d. None of the above

Choice (a.) is correct. A genetic test looks specifically for mutations within a certain gene. A negative genetic test result simply means that no mutations were detected in that specific gene by that specific test.

Choice (b.) is incorrect. A genetic test only looks at mutations within a certain gene. If the result is negative, there still may be mutations undetectable by that test, or in other genes that could cause genetic diseases.

Choice (c.) is incorrect. Genetic testing often cannot detect all disease-causing mutations. It is also possible that the patient has a genetic cause for disease which has not been discovered in the disease population.

Choice (d.) is incorrect. Answer (a.) is correct.

MODULE 5: INHERITED CONGENITAL ANOMALIES OF THE EYE

1. A congenital disorder is:
 - a. A disorder you get when you're older
 - b. A disorder you are born with**
 - c. A type of heart disease
 - d. A reproductive system disorder

Choice (a.) is incorrect. A congenital disorder is not a disorder you get or develop when you are older, it is something you are born with.

Choice (b.) is correct. A congenital disorder is a disease or malformation that you were born with and was present at the time of birth.

Choice (c.) is incorrect. A congenital disorder is not a type of heart disease. Disorders related to the heart are called cardiac disorders. A cardiac disorder may be congenital if an individual is born with it.

Choice (d.) is incorrect. A congenital disorder is not a reproductive system disorder.

2. An inherited congenital anomaly of the eye:
 - a. Must be found in multiple family members
 - b. Has a known genetic cause
 - c. Is never associated with other health problems
 - d. None of the above**

Choice (a.) is incorrect. An inherited congenital anomaly of the eye does not need to be found in any other family members. It may be a recessive or X-linked disorder for which parents may be unaffected carriers of the genetic change. However, having multiple affected family members does raise suspicion for a genetic eye disorder.

Choice (b.) is incorrect. An inherited congenital anomaly of the eye may or may not have a known genetic cause. Many of the genes which cause inherited congenital eye anomalies are yet unknown.

Choice (c.) is incorrect. An inherited congenital anomaly of the eye may be isolated (meaning the only manifestation) or syndromic (associated with other symptoms often including other parts of the body)

Choice (d.) is correct. None of the above answers are correct about an inherited congenital anomaly of the eye.

3. Approximately what percent of genetic diseases have eye abnormalities?
 - a. 8%
 - b. 20%
 - c. 33%**
 - d. 50%

Choice (a.) is incorrect. More than 8% of genetic disease have eye abnormalities.

Choice (b.) is incorrect. More than 20% of genetic disease have eye abnormalities.

Choice (c.) is correct. Approximately 1/3 or 33% of all genetic disease have eye abnormalities.

Choice (d.) is incorrect. Less than 50% of genetic disease have eye abnormalities.

4. A recurring pattern of anomalies that are the result of the same genetic cause is called a/an:

- a. Syndrome**
- b. Association
- c. Disruption
- d. Environmental effect

Choice (a.) is correct. A syndrome is defined as a recurring pattern of anomalies that are the result of the same underlying genetic cause. CHARGE is a syndrome because it may affect the eye, ear, heart, and other organ systems and it has a single underlying cause.

Choice (b.) is incorrect. An association is the occurrence of two or more anomalies together which are seen more often than expected by chance alone. Associations do not have a known underlying genetic cause.

Choice (c.) is incorrect. A disruption results from the destruction or loss of fetal tissue that would otherwise develop normally. One example is of a cause of disruption is amniotic bands.

Choice (d.) is incorrect. An environmental effect is when a condition or disease is either caused by or triggered by exposure to certain risk factors in our environment. If a disease is the result of a combination of genetic and environmental influences, this is called multifactorial.

5. An eye condition that is not associated with other health problems is:

- a. Syndromic
- b. Unique
- c. Isolated**
- d. Single

Choice (a.) is incorrect. A syndromic eye condition is one which IS associated with other health problems in the individual due to the same genetic cause.

Choice (b.) is incorrect. Unique is not a term used to describe an eye condition.

Choice (c.) is correct. An isolated eye condition means that the condition ONLY involves the eye and no other organ systems of the body.

Choice (d.) is incorrect. Single is not a term used to describe an eye condition. Single often is used to describe a single-gene disorder, meaning only one gene is involved.

6. A condition that shows a range of severity is called a/an:

- a. Spectrum**
- b. Association
- c. Assortment
- d. Field defect

Choice (a.) is correct. A condition which shows a spectrum is one which results in a range of severity or expression in individuals either in different families or within the same family.

Choice (b.) is incorrect. An association is the occurrence of two or more anomalies together which are seen more often than expected by chance alone. It does not speak to the severity of a condition.

Choice (c.) is incorrect. Assortment is the random distribution of genetic material from parents to children.

Choice (d.) is incorrect. A field defect refers to a disturbance or problem in the visual field, the full view seen by an eye that is fixating straight ahead.

7. Approximately what percent of the body's genes are expressed in the eye?
- a. 10%
 - b. 50%
 - c. 90%**
 - d. 100%

Choice (a.) is incorrect. Greater than 10% of the body's genes are expressed by cells in the eye.

Choice (b.) is incorrect. Greater than 50% of the body's genes are expressed by cells in the eye.

Choice (c.) is correct. 90% of the body's genes are expressed by cells in the eye.

Choice (d.) is incorrect. Less than 100% of the body's genes are expressed by cells in the eye.

8. A gene mutation that results in a congenital eye anomaly is:
- a. Not able to be found, even with genetic testing
 - b. Only in the cells of the eye
 - c. Only in parts of the body where a person has health problems
 - d. In every cell of the body**

Choice (a.) is incorrect. A genetic test may be able to identify a gene mutation for a congenital eye anomaly.

Choice (b.) is incorrect. The genetic mutation which causes a congenital eye anomaly is typically present in every cell of the body, not only in the cells of the eye.

Choice (c.) is incorrect. The genetic mutation which causes a congenital eye anomaly is typically in every cell of the body, not just the affected body part.

Choice (d.) is correct. The genetic mutation which causes a congenital eye anomaly is present in every cell of the body, not just in the eye.

9. What percent of pediatric blindness is due to a genetic cause?
- a. Less than 5%
 - b. 25%
 - c. 50%**
 - d. 80%

Choice (a.) is incorrect. More than 5% of pediatric blindness is due to a genetic cause.

Choice (b.) is incorrect. More than 25% of pediatric blindness is due to a genetic cause.

Choice (c.) is correct. Approximately half or 50% of pediatric blindness is due to a genetic cause.

Choice (d.) is incorrect. The genetic cause of pediatric blindness is less than 80%.

10. A person does not have an inherited eye condition if:
- They have a healthy eye exam as a baby
 - Their family members do not have eye problems
 - Their genetic testing is negative
 - None of the above**

Choice (a.) is incorrect. A healthy eye exam as an infant does not rule out an inherited eye condition. For example, retinitis pigmentosa is an inherited eye disease which can onset after childhood.

Choice (b.) is incorrect. Having a family history in which no family members have eye problems does not rule out an inherited condition in the patient.

Choice (c.) is incorrect. A negative genetic test does not rule out an inherited eye condition in the patient.

Choice (d.) is correct. None of the above statements are correct about an inherited eye condition.

11. Leber's Congenital Amaurosis (LCA) is an example of an inherited eye disease that may be caused by:
- One mutation in all patients
 - One gene in all patients
 - Many genes that differ among patients**
 - Environmental exposures

Choice (a.) is incorrect. There is no one mutation that is responsible for all patients' LCA. It can be caused by many mutations.

Choice (b.) is incorrect. There is no one gene that is responsible for all patients' LCA. It can be caused by many genes.

Choice (c.) is correct. LCA can be caused by many different genes and different people with LCA may have different mutations in different genes.

Choice (d.) is incorrect. Environmental exposures do not cause LCA.

12. Retinitis Pigmentosa (RP) is a genetic eye disease that is passed down in a/an:
- Autosomal dominant trait
 - Autosomal recessive trait
 - X-linked trait
 - All of the above**

Choice (a.) is incomplete. Retinitis pigmentosa can be passed through a family as an autosomal dominant trait but it is not the only form of inheritance.

Choice (b.) is incomplete. Retinitis pigmentosa can be passed through a family as an autosomal recessive trait but it is not the only form of inheritance.

Choice (c.) is incomplete. Retinitis pigmentosa can be passed through a family as an X-linked trait but it is not the only form of inheritance.

Choice (d.) is correct. All of the above are forms of inheritance of retinitis pigmentosa (also includes mitochondrial)

13. Which of the following statements are true about retinoblastoma (RB)?
- a. All of the children of a parent with RB will be affected
 - b. A child can only be affected with RB if one of their parents is affected
 - c. RB can either be inherited or sporadic**
 - d. A parent with RB is not at risk to have an affected child

Choice (a.) is incorrect. Not all children of an affected parent will be affected. Retinoblastoma may be sporadic in the parent and not something they would pass on to their child. Also, even if it is an inherited form, there is only a 50% or 1 in 2 chance of passing on the responsible gene with dominant inheritance.

Choice (b.) is incorrect. A child does not need to have an affected parent in order to have retinoblastoma. Some individuals have a sporadic form in which the genetic changes are present only in that individual.

Choice (c.) is correct. Retinoblastoma may be either inherited in an autosomal dominant fashion (germline mutations) or sporadic, meaning the only individual in the family with the genetic changes in the tumor cells.

Choice (d.) is incorrect. A parent with retinoblastoma is at risk to have an affected child if they have an inherited form (germline mutation). They would have a 50% chance to pass on the responsible gene to any of their future children.

14. A congenital cataract is an example of an eye condition where:
- a. All of the underlying genetic causes are known
 - b. None of the genetic causes are known
 - c. Some of the genetic causes are known, and some are yet to be identified**
 - d. It is never genetic

Choice (a.) is incorrect. Many of the genetic causes of congenital cataract are still unknown.

Choice (b.) is incorrect.

Choice (c.) is correct. Some of the genetic causes of congenital cataract are known while some are yet unknown.

Choice (d.) is incorrect. There are known genetic causes for congenital cataract.

15. Leber's Hereditary Optic Neuropathy (LHON) is caused by:
- a. Nuclear gene mutations
 - b. Mitochondrial mutations**
 - c. Chromosome deletions
 - d. All of the above

Choice (a.) is incorrect. LHON is not caused by nuclear gene mutations.

Choice (b.) is correct. LHON is caused by mitochondrial DNA (mtDNA) mutations.

Choice (c.) is incorrect. LHON is not caused by chromosome deletions.

Choice (d.) is incorrect. One answer above (b.) is correct.

MODULE 6: TALKING TO A PATIENT I – PATIENT EDUCATION BASICS

1. A Genetic Educator should be:

- a. Sensitive
- b. Respectful
- c. Informative
- d. **All of the above**

Choice (a.) is incorrect. A Genetic Educator should be sensitive when speaking with a patient or family about health-related information. However, there are additional, helpful qualities listed above.

Choice (b.) is incorrect. A Genetic Educator should be respectful of a patient or family when providing care, particularly regarding their actions, values, and beliefs. However, there are additional, helpful qualities listed above.

Choice (c.) is incorrect. A Genetic Educator should be informative to a patient or family, providing a simplified explanation of genetic concepts. However, there are additional, helpful qualities listed above.

Choice (d.) is correct. All of these qualities are useful when interacting with a patient or family.

2. The goal of giving genetic information to a patient is:

- a. To teach them to be geneticists
- b. To show them how much you know
- c. **To help them better understand their own health**
- d. To cure their health problems

Choice (a.) is incorrect. It is not possible to teach a patient all of the scientific concepts and facts about genetics.

Choice (b.) is incorrect. It is not helpful to provide an excess of genetic information to a patient with the purpose of demonstrating your level of knowledge.

Choice (c.) is correct. Providing basic genetic information allows a patient to begin the process of understanding their health in the context of genetics.

Choice (d.) is incorrect. Regardless of the amount of genetic information provided to a patient, the information does not lead to a cure for their health problem.

3. Finding out about a genetic diagnosis can change a patient's:

- a. **Management and treatment**
- b. Culture
- c. Genes
- d. None of the above

Choice (a.) is correct. A genetic diagnosis may guide management and lead to treatment options, based on the underlying condition and its natural history.

Choice (b.) is incorrect. Learning about a genetic diagnosis does not change the characteristics that one learns from their culture or nation, such as values, beliefs, attitudes, or customs.

Choice (c.) is incorrect. A genetic diagnosis may result because a change in a person's genetic information; however, learning of the diagnosis does not cause a subsequent change in a person's genes.

Choice (d.) is incorrect. One of the above answers is correct (see answer a).



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4. Factors that will affect a patient's understanding of genetics include:

- a. Educational background
- b. Cultural practices
- c. Language barriers
- d. **All of the above**

Choice (a.) is incorrect. Educational background can affect a patient's understanding of genetics, particularly if they had limited schooling or did not have significant time spent in biology courses.

Choice (b.) is incorrect. A patient's cultural background and beliefs may affect the way they accept and interpret genetic information.

Choice (c.) is incorrect. Given the specialized care provided by ophthalmic clinics, your patient may speak a different language and have difficulty understanding technical, genetic terms in a less familiar language.

Choice (d.) is correct. All of the above factors will affect a patient's understanding of genetics.

5. When meeting with a patient, after you introduce yourself, the first thing you will do is:

- a. Give them a diagnosis
- b. Explain chromosomes
- c. **Take his or her family pedigree**
- d. Ask what their job is

Choice (a.) is incorrect. Providing a medical diagnosis is the responsibility of the examining physician. This is not required to provide basic genetic information to a patient.

Choice (b.) is incorrect. Although discussing chromosomes and genetic information may be relevant to a patient's situation, it is not the first topic that should be presented after meeting a patient.

Choice (c.) is correct. A family pedigree is one of the first tasks of a Genetic Educator because it provides an organized and detailed overview of the family's health.

Choice (d.) is incorrect. Knowing a patient's occupation is not relevant when providing basic genetics information.

6. When speaking with a patient, a Genetic Educator should:

- a. Speak in all medical/technical terms
- b. Tell the patient what to do
- c. Give the patient a diagnosis
- d. **Simplify concepts so they are easy to understand**

Choice (a.) is incorrect. Speaking in all medical/technical terms is the opposite of how a Genetic Educator should speak to a patient. It is unlikely for a patient to fully understand scientific terms relevant to genetics and using this language will make communicating this information more difficult.

Choice (b.) is incorrect. It is not the responsibility of a Genetic Educator to tell a patient what to do. A patient's autonomy, or ability to make informed decisions on their own, must be respected.

Choice (c.) is incorrect. Providing a medical diagnosis is the responsibility of the examining physician. This is not a responsibility or expectation of a Genetic Educator.

Choice (d.) is correct. Simplifying genetic information into easy to understand terms is an essential task of a Genetic Educator. Speaking slowly, clearly, and avoiding technical terms will allow a patient to understand genetic information relevant to their health.



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7. Terms that should be defined to patients include:

- a. Inherited
- b. Congenital
- c. Genetic Disorder
- d. **All of the above**

Choice (a.) is incorrect. A patient may not understand the term “inherited,” and it must be explained so that they can understand potential inheritance patterns. However, It is very likely that there are many technical or medical terms a patient may not understand.

Choice (b.) is incorrect. A patient may not understand the term “congenital,” and it must be explained so that they can understand the onset of particular conditions. However, It is very likely that there are many technical or medical terms a patient may not understand.

Choice (c.) is incorrect. A patient may not understand “genetic disorder,” and it must be explained so that they can understand certain diagnoses provided by an examining physician. However, It is very likely that there are many technical or medical terms a patient may not understand.

Choice (d.) is correct. All of the above terms, and likely many others, must be defined for patients so that they can understand the information provided.

8. When should patients be allowed to ask questions?

- a. Never during the session
- b. **At any time during the conversation**
- c. Only at the beginning of the meeting
- d. Only at the end of the meeting

Choice (a.) is incorrect. It is unrealistic to expect a patient to understand all of the information provided, without having the need or desire to ask a question.

Choice (b.) is correct. In order to maximize the benefit of providing genetic information, a patient should be allowed and encouraged to ask questions during a session.

Choice (c.) is incorrect. A patient may not know what to expect from a Genetic Educator and is unlikely to have questions related to genetics prior to a session. Additionally, their questions may be addressed at some point during the session, which does not maximize the usefulness of the time spent with a patient.

Choice (d.) is incorrect. It may be less helpful for a patient to hold their questions until the end of a session, because they may have limited understanding that could be addressed or forget the question they wanted to ask.

9. If the Genetic Educator does not know the answer to a patient's question, he or she should:

- a. **Be honest and encourage the patient to ask their ophthalmologist**
- b. Make up an answer to appear informed
- c. Not respond
- d. None of the above

Choice (a.) is correct. It is not realistic or expected for a Genetic Educator to have an answer to every patient question. If you do not know the answer to a patient's question, it is best to say that you do not know, but the ophthalmologist may have a response.

Choice (b.) is incorrect. It is not appropriate to make up an answer to a patient's question, particularly because this misinformation may affect their understanding of genetics or family health history.

Choice (c.) is incorrect. It is disrespectful to ignore a patient's question or request.

Choice (d.) is incorrect. One of the above answers is correct (see choice a).

10. If the patient needs more help understanding a certain topic, a Genetic Educator should:

- a. Use names and diagnoses of other patients as examples
- b. Keep talking and hope that if they hear more they will understand
- c. **Have the patient ask the ophthalmologist for more information**
- d. Start over from the beginning

Choice (a.) is incorrect. It is not appropriate to use other patient's names and diagnoses to help a person understand genetic information. It is your responsibility to keep such information private.

Choice (b.) is incorrect. If a patient has difficulty with a particular topic, it is unlikely that further, detailed explanations will allow them to understand it more clearly. Rather, this may become frustrating for a patient and have the opposite effect.

Choice (c.) is correct. Given the limited amount of information addressed during a session, it is best to direct further questions to the patient's ophthalmologist.

Choice (d.) is incorrect. It is not helpful to review all of the information covered during a session in order to help a patient understand a particular topic. Also, given the potential time limitations in clinic, starting a session from the beginning will only waste time and likely not lead to better understanding.

11. Taking a pedigree is important because:

- a. **It is a visual tool that may aid in diagnosis and inheritance pattern identification**
- b. It quizzes the patient
- c. It provides all of the information necessary to make a genetic diagnosis
- d. None of the above

Choice (a.) is correct. A pedigree is a visual tool that demonstrates how individuals in a family are related and lists each person's health problems. Having an overview of the family may link together diagnoses and demonstrate a particular inheritance pattern; however, this is not true of all pedigrees.

Choice (b.) is incorrect. The purpose of a pedigree is not to quiz the patient about their relatives and the family health history.

Choice (c.) is incorrect. It is not possible for a pedigree to provide all of the information for an ophthalmologist to make a genetic diagnosis. Many genetic diagnoses are based on clinical examinations or blood tests, which are supplemented by the information on a pedigree.

Choice (d.) is incorrect. One of the above answers is correct (see choice a)

12. Pedigrees include useful information for a:

- a. Patient
- b. Patient's family
- c. Ophthalmologist
- d. **All of the above**

Choice (a.) is incorrect. A pedigree includes important information for a patient; however, it is also useful to other individuals.

Choice (b.) is incorrect. A pedigree includes important information for a patient's family; however, it is also useful to other individuals.

Choice (c.) is incorrect. A pedigree includes important information for an ophthalmologist; however, it is also useful to other individuals.

Choice (d.) is correct. A pedigree includes important information for many people. A patient, family, and ophthalmologist can use it to understand and visualize the health problems in a family and potentially reveal an inheritance pattern.

13. After taking a pedigree, a Genetic Educator should:
- Put it in the patient's file**
 - Throw it away
 - Give the only copy to the patient to take home
 - Keep it for your reference

Choice (a.) is correct. A completed pedigree should be put in the patient's file so that the ophthalmologist can refer to it and add further information during the appointment and future visits.

Choice (b.) is incorrect. It is not appropriate to collect health information without purpose. Also, the pedigree is an important piece of understanding a family's health history and it should be maintained and stored for reference and interpretation.

Choice (c.) is incorrect. Although a patient may request a copy of their pedigree, the original should be stored in the clinic for reference and interpretation.

Choice (d.) is incorrect. It is appropriate to share the pedigree with the ophthalmologist, as it may provide information relevant to a patient's diagnosis and care.

14. When speaking with a patient, a Genetic Educator should:
- Talk as fast as possible to get to the next patient
 - Talk clearly so the patient can understand**
 - Skip over information that you do not think is important
 - Talk about yourself

Choice (a.) is incorrect. It is not respectful to speak with patients as fast as possible. This is unlikely to lead to good understanding of genetic information.

Choice (b.) is correct. It is helpful to speak clearly when providing genetic information to minimize a patient's misunderstanding.

Choice (c.) is incorrect. It is not the responsibility of a Genetic Educator to determine what information is relevant to a patient or their diagnosis.

Choice (d.) is incorrect. It is not appropriate for a Genetic Educator to provide personal information about themselves to a patient.

15. An effective communicator:
- Actively listens
 - Speaks in a way that aids the understanding of other people
 - Is confident about the information they are presenting
 - All of the above**

Choice (a.) is incorrect. Active listening – the process of listening, responding, and understanding a person who is speaking – is an important skill. However, there are additional traits that lead to effective communication.

Choice (b.) is incorrect. Speaking in a way that leads to improved patient's understanding is an important skill. However, there are additional traits that lead to effective communication.

Choice (c.) is incorrect. It is important to understand and have confidence in the information that is presented. However, there are additional traits that lead to effective communication.

Choice (d.) is correct. All of the above skills are important for effective communication.

MODULE 7: TALKING TO A PATIENT II – TAKING A FAMILY PEDIGREE

1. A useful family history should include ____ generations of information:

- a. 1
- b. 2
- c. **3**
- d. Does not matter

Choice (a.) is incorrect. Including only one generation in a family history is not useful because it only documents the health information of a patient and their brothers and sisters. This limited history would not allow accurate identification of potential inheritance patterns.

Choice (b.) is incorrect. Including only two generations (children and parents/aunts/uncles/cousins) in a family history may lack important information, especially for X-linked conditions where more distant generations may display related health problems. Having information about further generations can be very important in interpreting a family history.

Choice (c.) is correct. Including three generations in a family history is most useful because it will help allow for interpretation of inheritance patterns. Demonstrating the health status of grandchildren through grandparents will provide the ophthalmologist with the most complete history from which to determine inheritance patterns.

Choice (d.) is incorrect. It is important to include 3 generations as part of a family history in order to make it most useful to the ophthalmologist.

2. When taking a family pedigree, an arrow is drawn to the symbol representing:

- a. The oldest individual in the family
- b. The youngest individual in the family
- c. All individuals affected with a disorder
- d. **The current patient**

Choice (a.) is incorrect. The oldest individual in the family may not be relevant to the reasons a family history is recorded, regardless of their health.

Choice (b.) is incorrect. The youngest individual in the family may not be relevant to the reasons a family history is recorded, regardless of their health.

Choice (c.) is incorrect. All individuals affected with a specific disorder are identified by shading, or filling in, their respective symbols with a pattern. An arrow is not used for this reason.

Choice (d.) is correct. An arrow in a pedigree is drawn to indicate the current patient, also known as the proband.

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3. Useful information to include for each person on a family pedigree is:

- a. Age
- b. Any vision problems
- c. Any diagnoses of eye disorders
- d. **All of the above**

Choice (a.) is incorrect. Although documenting age is important information on a family pedigree, especially when recording an age at diagnosis or death, it is not the only information to be documented.

Choice (b.) is incorrect. In the ophthalmology clinic, it is important to document the vision problems of family members; however, there is additional health information that should be documented.

Choice (c.) is incorrect. In the ophthalmology clinic, it is important to document diagnosed eye conditions; however, there is additional health information that should be documented.

Choice (d.) is correct. When obtaining a family pedigree, it is important to document age of the individual as well as age of diagnosis or death, any vision problems, and any diagnoses of eye disorders for each person in the family.

4. On a pedigree, a line represents a:

- a. Person
- b. Pregnancy
- c. **Familial relationship**
- d. None of the above

Choice (a.) is incorrect. A person or individual in a pedigree is represented by a symbol. Specifically, squares indicate males, circles indicate females, and diamonds indicate individuals where the gender is unknown (for example: distant relatives, etc.).

Choice (b.) is incorrect. A pregnancy is indicated by a symbol with the letter "P" written inside. If the gender of the pregnancy is known, the symbol can reflect this (squares for males, circles for females). If the gender of the pregnancy is not yet known, a diamond should be used.

Choice (c.) is correct. All relationships within a pedigree are represented by a line. Marriages or couples are indicated by a horizontal line, and children are connected to a couple using a vertical line. If there are multiple children, the vertical line is branched to show that they are all related through the same parents.

Choice (d.) is incorrect. One of the above answers is correct (see choice c).

5. On a pedigree, a male is represented by a:

- a. Circle
- b. **Square**
- c. Triangle
- d. Diamond

Choice (a.) is incorrect. A female is represented by a circle

Choice (b.) is correct. A male is represented by a square.

Choice (c.) is incorrect. A miscarriage is represented by a triangle.

Choice (d.) is incorrect. Individuals of unknown gender are represented by a diamond.

6. On a pedigree, a female is represented by a:

- a. **Circle**
- b. Square
- c. Triangle
- d. Diamond

Choice (a.) is correct. A female is represented by a circle.

Choice (b.) is incorrect. A male is represented by a square.

Choice (c.) is incorrect. A miscarriage is represented by a triangle.

Choice (d.) is incorrect. Individuals of unknown gender are represented by a diamond.

7. On a pedigree, a miscarriage is represented by a:

- a. Circle
- b. Square
- c. **Triangle**
- d. Diamond

Choice (a.) is incorrect. A male is represented by a square.

Choice (b.) is incorrect. A female is represented by a circle.

Choice (c.) is correct. A miscarriage is represented by a triangle.

Choice (d.) is incorrect. Individuals of unknown gender are represented by a diamond.

8. When two parents are related by blood, their relationship is depicted by:

- a. A single horizontal line
- b. **A double horizontal line**
- c. A vertical line
- d. A diagonal line




Choice (a.) is incorrect. A single horizontal line represents a relationship where the two individuals (parents) are not related by blood.

Choice (b.) is correct. A double horizontal line represents a relationship where the two individuals (parents) are related by blood.

Choice (c.) is incorrect. A vertical line represents the familial relationship between parents and children.

Choice (d.) is incorrect. A diagonal line through a symbol indicates that the individual is deceased. Diagonal lines from a common point represent individuals who are twins.

9. Which symbol is used for a female carrier (unaffected, heterozygous) of an autosomal recessive or X-linked disorder?

- a. 
- b. 
- c. 
- d. 

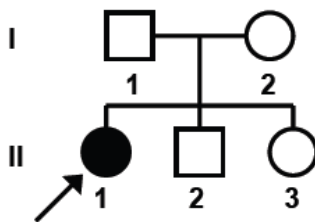
Choice (a.) is correct. A female is represented by a circle and an unaffected carrier is identified by a dot within the symbol.

Choice (b.) is incorrect. A female is represented by a circle. However, there is no indication that this female is an unaffected carrier of a genetic condition. Carriers are identified on a pedigree by a dot within a symbol.

Choice (c.) is incorrect. A male is represented by a square. This symbol is shaded, indicating that this male is affected with a condition or genetic disorder.

Choice (d.) is incorrect. A female is represented by a circle. This symbol is shaded, indicating that this female is affected with a condition or genetic disorder.

Use the following pedigree to answer questions 10 and 11.



10. In the above pedigree, which individual is the proband?

- a. I-1
- b. I-2
- c. II-1
- d. II-3

Choice (a.) is incorrect. I-1 is the proband's father. The proband is indicated by the arrow.

Choice (b.) is incorrect. I-2 is the proband's mother. The proband is indicated by the arrow.

Choice (c.) is correct. II-1 is the proband, indicated by the arrow.

Choice (d.) is incorrect. II-3 is the proband's sister. The proband is indicated by the arrow.

11. In the above pedigree, what is the relationship between II-2 and II-3?

- a. Husband and wife
- b. **Siblings**
- c. Half siblings
- d. Father and daughter

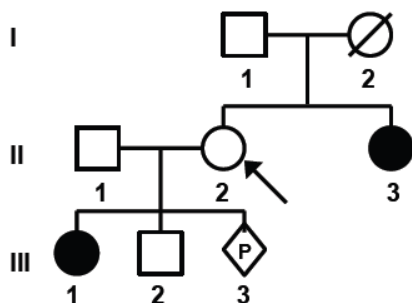
Choice (a.) is incorrect. A husband and wife relationship is depicted using a single horizontal line. In this pedigree, individuals I-1 and I-2 are husband and wife.

Choice (b.) is correct. Individuals II-2 and II-3 are siblings (brother and sister). This is depicted using branching vertical lines from the parents (I-1 and I-2).

Choice (c.) is incorrect. Half-siblings are not directly connected with horizontal or vertical lines. Half-siblings would be connected through their common parent on separate vertical lines from each other. There are no half-siblings shown in this pedigree.

Choice (d.) is incorrect. A father and daughter relationship is depicted using a vertical line (if an only child) or a branched vertical line (if there are multiple children). In this pedigree, individual I-1 is the father and individuals II-1 and II-3 are his daughters.

Use the following pedigree to answer questions 12-15.



12. In the above pedigree, which individual is deceased?

- a. I-1
- b. **I-2**
- c. III-1
- d. III-3

Choice (a.) is incorrect. Individual I-1 is living. On a pedigree, a diagonal line through a symbol indicates that the individual is deceased.

Choice (b.) is correct. Individual I-2 is deceased. On a pedigree, a diagonal line through a symbol indicates that the individual is deceased.

Choice (c.) is incorrect. III-1 is living and affected with a condition or genetic disorder, indicated by shading. On a pedigree, a diagonal line through a symbol indicates that the individual is deceased.

Choice (d.) is incorrect. III-3 is a current pregnancy (indicated by "P") where the gender is not yet known. On a pedigree, a diagonal line through a symbol indicates that the individual is deceased.

13. In the above pedigree, how many current children does the patient (II-2) have?

- a. 0
- b. 1
- c. 2
- d. 3

Choice (a.) is incorrect. The patient (II-2) has children. This relationship is represented by the descending and branched vertical line. An individual without children will not be connected to other symbols with a descending vertical line.

Choice (b.) is incorrect. The patient (II-2) has children. This relationship is represented by the descending and branched vertical line. An individual with one child will be connected to the child's symbol by a single vertical line.

Choice (c.) is correct. The patient (II-2) has two current children and one pregnancy. This relationship is represented by the descending and branched vertical line.

Choice (d.) is incorrect. The patient (II-2) does not have three children. Rather, the patient has two current children and one pregnancy (represented by the diamond with the letter "P").

14. In the above pedigree, what is the relationship between I-1 and III-2?

- a. Grandfather and grandson
- b. Grandmother and granddaughter
- c. Uncle and niece
- d. Uncle and nephew

Choice (a.) is correct. Individuals I-1 and III-2 are related as a grandfather and grandson. This is most easily recognized by their generation numbers (I and III), and that they are separated by a full generation (generation II). Also, both individuals are male, as indicated by squares.

Choice (b.) is incorrect. Individuals I-1 and III-2 are not related as a grandmother and granddaughter. Although the generational separation is correct, I-1 and III-2 are males, as indicated by squares.

Choice (c.) is incorrect. Individuals I-1 and III-2 are not related as an uncle and niece. An uncle and niece would be separated by a single generation (not demonstrated in this pedigree) and both I-1 and III-2 are males, where a niece would be female and represented by a circle.

Choice (d.) is incorrect. Individuals I-1 and III-2 are not related as an uncle and nephew. An uncle and nephew would be separated by a single generation (not demonstrated in this pedigree).

15. In the above pedigree, what is III-3?

- a. A son of II-2
- b. A daughter of II-2
- c. An unborn child (pregnancy) of II-2
- d. None of the above

Choice (a.) is incorrect. Because III-3 is demonstrating a diamond with a P in the center, we know that this is an unborn child. Sons are represented by a square from a descending vertical line. The son of II-2 is III-2; he is unaffected because he is not shaded.

Choice (b.) is incorrect. Because III-3 is demonstrating a diamond with a P in the center, we know that this is an unborn child. Daughters are represented by a circle from a descending vertical line. The daughter of II-2 is III-1; she is affected because she is shaded.

Choice (c.) is correct. The symbol, a diamond with the letter P in the center represents the unborn child (pregnancy) of II-2, the mother.

Choice (d.) is incorrect. One answer above is correct (see answer c).

APPENDIX F

QUESTIONNAIRES

F.1 DEMOGRAPHIC QUESTIONNAIRE

1. Education: _____
2. Title in workplace: _____
3. Number of years employed at current workplace: _____
4. Average **total** number of patients seen per day at clinic: _____
5. Average number of patients **you** see per day: _____
6. How would you rank your knowledge of genetics?
 - a. No Knowledge
 - b. Very Poor
 - c. Poor
 - d. Satisfactory
 - e. Good
 - f. Very Good
7. Have you received any formal genetics education?
 - a. Yes If yes, please describe: _____
 - b. No
8. Do you know of a genetics clinic in your institution?
 - a. Yes
 - b. No
9. In general, how comfortable do you feel with dealing with genetics issues with your patients?
 - a. Very Comfortable
 - b. Comfortable
 - c. Neither comfortable nor uncomfortable
 - d. Uncomfortable
 - e. Very Uncomfortable

10. How often do you complete a family history for a new patient?
- a. Never
 - b. Sometimes
 - c. Often
 - d. Always
11. In your practice, how often do you discuss genetics with a patient?
- a. Never
 - b. Only if the patient has a genetic condition
 - c. Occasionally, but only if there seems to be good reason for it
 - d. Often, whenever it seems appropriate
 - e. Mostly, it is my usual practice
 - f. Almost always, with almost all patients when taking a medical history

F.2 FOLLOW-UP QUESTIONNAIRES

The following questionnaire was administered at 3 time points: post-course, post-workshop, and post-implementation (final).

1. Average **total** number of patients seen per day at clinic: _____
2. Average number of patients **you** see per day: _____
3. How would you rank your knowledge of genetics?
 - a. No Knowledge
 - b. Very Poor
 - c. Poor
 - d. Satisfactory
 - e. Good
 - f. Very Good
4. Now, in general, how comfortable do you feel with dealing with genetics issues with your patients?
 - a. Very Comfortable
 - b. Comfortable
 - c. Neither comfortable nor uncomfortable
 - d. Uncomfortable
 - e. Very Uncomfortable
5. How often do you complete a family history for a new patient?
 - a. Never

- b. Sometimes
 - c. Often
 - d. Always
6. In your practice, how often do you discuss genetics with a patient?
- a. Never
 - b. Only if the patient has a genetic condition
 - c. Occasionally, but only if there seems to be good reason for it
 - d. Often, whenever it seems appropriate
 - e. Mostly, it is my usual practice
 - f. Almost always, with almost all patients when taking a medical history

Directions: Please choose the number that best represents your attitude toward the corresponding statement. 1 = Strongly Disagree; 2 = Moderately Disagree; 3 = Neutral/Don't Know; 4 = Moderately Agree; 5 = Strongly Agree

Example 1: I live in the country of India.

| | | | | | | |
|-------------------|---|---|---|---|---|----------------|
| Strongly disagree | 1 | 2 | 3 | 4 | 5 | Strongly agree |
|-------------------|---|---|---|---|---|----------------|

Example 2: I like American football.

| | | | | | | |
|-------------------|---|---|---|---|---|----------------|
| Strongly disagree | 1 | 2 | 3 | 4 | 5 | Strongly agree |
|-------------------|---|---|---|---|---|----------------|

1. This training program advanced my professional development.

| | | | | | | |
|-------------------|---|---|---|---|---|----------------|
| Strongly disagree | 1 | 2 | 3 | 4 | 5 | Strongly agree |
|-------------------|---|---|---|---|---|----------------|

2. This training program increased my knowledge and understanding of genetics.

| | | | | | | |
|-------------------|---|---|---|---|---|----------------|
| Strongly disagree | 1 | 2 | 3 | 4 | 5 | Strongly agree |
|-------------------|---|---|---|---|---|----------------|

3. This training program helped me to communicate basic inheritance patterns to patients.

| | | | | | | |
|-------------------|---|---|---|---|---|----------------|
| Strongly disagree | 1 | 2 | 3 | 4 | 5 | Strongly agree |
|-------------------|---|---|---|---|---|----------------|

4. I feel confident in my ability to provide basic genetic education to patients.

| | | | | | | |
|-------------------|---|---|---|---|---|----------------|
| Strongly disagree | 1 | 2 | 3 | 4 | 5 | Strongly agree |
|-------------------|---|---|---|---|---|----------------|

5. Providing patients with basic genetic education fits into the workflow of our clinic.

| | | | | | | |
|-------------------|---|---|---|---|---|----------------|
| Strongly disagree | 1 | 2 | 3 | 4 | 5 | Strongly agree |
|-------------------|---|---|---|---|---|----------------|

6. Basic genetic education benefits the patients to whom I provide it.

| | | | | | | |
|-------------------|---|---|---|---|---|----------------|
| Strongly disagree | 1 | 2 | 3 | 4 | 5 | Strongly agree |
|-------------------|---|---|---|---|---|----------------|

7. It is important for me to stay current on fundamental information on inherited genetic diseases of the eye.

| | | | | | | |
|-------------------|---|---|---|---|---|----------------|
| Strongly disagree | 1 | 2 | 3 | 4 | 5 | Strongly agree |
|-------------------|---|---|---|---|---|----------------|

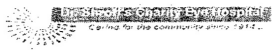
APPENDIX G

CERTIFICATE OF COMPLETION



APPENDIX H

DR SHROFF CHARITY EYE HOSPITAL PEDIGREE FORM



Genetic Educator Clinic 3 Generation Pedigree chart

| | | | |
|-----------|-------------|----------|-------------|
| Name | Age/Sex | MR No | Date & Time |
| Diagnosis | Referred By | Educator | Remarks |
| Historian | Contact No | Location | Visit No |

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